

**TIMING AND COORDINATION OF GAIT: IMPACT OF AGING, GAIT SPEED AND  
RHYTHMIC AUDITORY CUEING**

by

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University of Pittsburgh, 2016

**Purpose:** The aims of this dissertation were to: 1) compare the test-retest reliability and determine minimal detectable change (MDC) of spatial and temporal gait variability in younger and older adults 2) examine the impact of challenging walking conditions (slower and faster speeds) on gait variability in younger and older adults and 3) examine the impact of rhythmic auditory cueing (metronome) on the walk ratio as an indicator of the spatial and temporal coordination of gait at different walking speeds in healthy adults.

**Subjects:** Forty younger (mean age =  $26.6 \pm 6.0$  years) and 120 older adults (mean age =  $78.1 \pm 6.2$  years) independent in ambulation were studied.

**Methods:** Gait characteristics were collected using a computerized walkway (GaitMat II™). Step length, step width, step time, swing time, stance time and double support time variability were derived as the standard deviation of all steps across the 4 passes. Cadence and walk ratio were also calculated.

**Analyses:** Test-retest reliability was calculated using Intra-class correlation coefficients ( $ICCs_{(2,1)}$ ), relative limits of agreement (LoA%) and standard error of measurement (SEM). The MDC at 90% and 95% level were also calculated. Mixed linear models were used to determine differences in gait variability between younger and older by walking conditions and with metronome cues.

**Results and Clinical Relevance:** Younger adults had greater test-retest reliability and smaller MDC of spatial and temporal gait variability compared to older adults. In older adults, walking slowly is more challenging to the motor control of gait and may be more sensitive to age-related declines in gait than usual and faster speed walks. Finally, a metronome-cue, commonly used in gait rehabilitation, may have been detrimental to the walking pattern. It is possible that the metronome-cue disrupts gait timing by increasing the attentional demand of walking at non-ideal speeds such as slower and faster speeds. Future research should further investigate inconsistency of gait variability as a potential early indicator of a decline in mobility. Also, future longitudinal studies are needed to determine if changes in gait variability on challenging gait conditions predict future mobility disability in older adults with near normal gait.

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## PREFACE

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## **1.0 INTRODUCTION**

Gait is an important human function that promotes independence and augments health. Under usual unconstrained conditions, walking appears to remain relatively constant from one step to the next.<sup>1</sup> This optimization of walking at usual speed is likely due to the inherent interaction of neural and biomechanical mechanisms, with only minimal active control of high-level sensory feedback control (i.e. good timing and coordination).

The timing and coordination of gait can be quantified using footfall measures,<sup>2</sup> smoothness of walking,<sup>3</sup> biomechanics measures<sup>4</sup> and energy cost of walking.<sup>5</sup> The focus of this dissertation will be on footfall measures, such as mean spatial and temporal characteristics and spatial and temporal gait variability, as a way to describe the timing and coordination of gait.

The major aim of this dissertation was to advance our knowledge about the timing and coordination of gait. There are different intrinsic and extrinsic factors that have the potential to influence the estimate of spatial and temporal characteristics of gait, such as characteristics of gait testing protocol (testing protocol, challenging walking conditions and external rhythmic auditory), characteristics of subject (aging and pathology), and characteristics of tester (walking instructions and data processing). Specifically, we set out to examine the impact of factors such as aging, challenging walking conditions (slower and faster speeds) and external rhythmic cueing (metronome).

Test-retest reliability is a fundamental psychometric requirement for any measure. However, in older adults the reliability of spatial and temporal gait is not well-established.<sup>6,7</sup> Lack of knowledge of the reliability measure limits the interpretation of gait variability.<sup>6</sup> In this regard, it is also important to know the minimal detectable change (MDC) to support the use of gait variability as an outcome measure in clinical or research settings.<sup>8</sup>

In older adults, some age-related decline in the organization and stability of the gait cycle is expected, which may be indicative of the overall health and control of the locomotor system. Little is known about age-related changes in spatial and temporal gait variability during challenging walking conditions such as slower and faster pace walking. It is likely that these challenging walks place a greater demand on motor control of gait and hence may be more sensitive to age-related declines in gait compared to usual walking speed.<sup>9,10</sup>

Rhythmic auditory cueing has had positive effects for improving spatio-temporal features of gait of patients with neurological disorders including Parkinson disease, stroke and hemiparesis.<sup>11-14</sup> For instance, in patients with Parkinson's disease synchronizing steps with rhythmic auditory cueing significantly improved walking speed, stride length and cadence.<sup>15</sup> However, it is difficult to completely interpret the influence of rhythmic auditory cueing on the timing and coordination of abnormal gait without first understanding the induced effects in healthy adults in the absence of aging and pathology.

### **1.1.1 Specific aim I**

To compare the test-retest reliability and determine minimal detectable change (MDC) of spatial and temporal gait variability in younger and older adults.

#### **1.1.1.1 Hypothesis I**

We hypothesized that younger adults will have greater test-retest reliability and smaller MDC of spatial and temporal gait variability compared to older adults.

#### **1.1.2 Specific aim II**

To examine the impact of challenging over-ground walking conditions (slower and faster speeds) on spatial and temporal gait variability in younger and older adults.

##### **1.1.2.1 Hypothesis II**

We expected gait variability would be greater under challenging walking conditions of slower and faster speeds compared to usual speed, and the impact would be greater in older adults compared to younger adults.

#### **1.1.3 Specific aim III**

To examine the impact of rhythmic auditory cueing (metronome) on the walk ratio as an indicator of the spatial and temporal coordination of gait at different walking speeds in healthy adults.

### **1.1.3.1 Hypothesis III**

Our hypothesis was that the walk ratio will deviate from the optimal value at slower and faster speeds compared to usual preferred walking speed. With changing speed (i.e. walking slower or faster than usual preferred speed), the metronome cues would facilitate a consistent ratio between step length and cadence.

## **2.0 BACKGROUND**

### **2.1 GAIT VARIABILITY**

#### **2.1.1 Preamble**

Variability is a natural feature of behavior of an organism.<sup>16</sup> Most physiological systems show complex variability when they are measured on a moment-to-moment or beat-to-beat basis, such as blood pressure (BP), heart rate (HR), brain electrical activity, and hormone concentration.<sup>17</sup> In human movement, variability is one of the most common features.<sup>18</sup> Human movement variability can be described as the normal variations that occur in motor performance across multiple repetitions of a task.<sup>19</sup> Bernstein (1967) used an expression “repetition without repetition” whereby each repetition of an act involved unique, non-repetitive neural and motor patterns.<sup>20</sup>

Gait parameters like most physiological signals are naturally fluctuating around a mean value on a step to step basis.<sup>21,22</sup> Gait variability is a quantifiable feature of walking defined as fluctuations in the spatial and temporal gait characteristics from one step or stride to the next. Under normal conditions in healthy adults, these fluctuations are relatively small reflecting remarkable consistency and stability within the locomotor system.<sup>1</sup> However, these fluctuations in spatio-temporal gait characteristics are altered in normal aging,<sup>23-25</sup> in certain disorders that are

largely considered having difficulties in the motor control of gait (i.e. Parkinson's and Alzheimer disease)<sup>26,27</sup> as well as in subclinical conditions.<sup>21,28,29</sup> Measures of gait variability may provide additional insights about mobility dysfunction and fall risk in older adults, above and beyond mean values of gait parameters such as average gait speed or step time.<sup>6,30,31</sup> In this sense, measures of spatial and temporal gait variability are becoming important clinical tools in older adults.<sup>32</sup>

This section reviews the literature on quantification and measurement methods of gait variability, age-related changes in gait variability, clinical significance of gait variability and neural origins of gait variability.

### **2.1.2 Gait cycle**

Gait is an important human function that plays an essential role in our daily physical activities. Normal human gait consists of consecutive gait cycles. Each gait cycle consists of a sequence of events containing both stance and swing phase. Stance phase is the time when the foot is in contact with the ground and represents approximately 60% of the gait cycle. The swing phase is when the foot is non-weight bearing and represents approximately 40% of the gait cycle. The stance phase is divided into load response phase, double support phase, mid stance phase, and terminal stance. The swing phase is divided into initial swing, mid-swing, and the terminal swing phase.<sup>33</sup>

Gait may be quantified by using kinematic and kinetic variables. Kinematic variables are used to describe movement not taking into account the forces that cause the movement, and may be linear or angular. Kinetic variables are used to describe the forces and moments that cause a

movement such as gravitational, ground reaction, other external forces, or forces produced by muscle contractions.<sup>34</sup> Our focus in this review will be on the linear kinematic parameter (spatio-temporal parameters).

### **2.1.3 Definition of spatial and temporal parameters of gait**

The spatial and temporal parameters of walking are commonly used to describe normal and pathological gait.<sup>35</sup> Spatial and temporal parameters are useful for both clinicians and researchers to identify gait deviations, make physical therapy diagnoses, determine appropriate therapy and monitor patient progress. The temporal components are those periods of time during which events take place such as step time. The spatial components refer to the position and orientation of limbs and joints such as step length.<sup>36</sup> There is a general agreement on the definitions of most gait parameters, including step length, step time, swing time and double support time, although less clarity about step width.<sup>37</sup> Definitions of the spatial and temporal parameters are listed in Table 1.

Additionally, when performing gait analysis, it is important to consider spatial and temporal aspects, since a disease or trauma can affect the gait spatial and temporal components independently.<sup>38</sup> Prior to exploring the different aspects of spatial and temporal characteristics of gait variability and their clinical significance, it is necessary to briefly discuss the common ways to quantify and measure gait variability.

**Table 1. Descriptions of spatial and temporal gait characteristics.**

<b>Gait Characteristics</b>	<b>Description</b>
<b>Spatial parameters</b>	
<b>Step length</b>	Distance between 2 consecutive footprints, measured from the heel of 1 footprint to the heel of the next footprint and was recorded in meters.
<b>Step width</b>	Distance between the outermost borders of 2 consecutive footprints and was recorded in meters.
<b>Temporal parameters</b>	
<b>Step time</b>	Time between initial foot-floor contact of one foot to the initial foot-floor contact of the contralateral side, recorded in seconds.
<b>Stance time</b>	Amount of time 1 foot is in contact with the floor (i.e. from initial foot-floor contact until final foot-floor contact), recorded in seconds.
<b>Swing time</b>	Time elapsed between the last contacts of the current footfall to the initial contact of the next footfall of the same foot, recorded in seconds.
<b>Double support time</b>	Double support occurs when both feet are in contact with the ground simultaneously; double support time is the sum of the time elapsed during two periods of double support in the gait cycle, recorded in seconds.
<b>Cadence (steps/min)</b>	The number of steps per minute.
<b>Spatiotemporal parameters</b>	
<b>Gait speed (m/s)</b>	Calculated by dividing the distance walked by the ambulation time.



#### 2.1.4 Quantification of gait variability

Currently, there is no gold standard to quantify gait variability, and a number of different statistical measures have been used.<sup>1,39</sup> The most common ways for estimating gait variability are within subject standard deviation,<sup>7,40,41,42-44</sup> and the coefficient of variation,<sup>2,21,29,30,45-47</sup> and some studies include both.<sup>48,49</sup>

The standard deviation calculates the degree by which individual scores vary from the mean. It is expressed in the same units as the measured data therefore providing an estimate of gait parameter's relative variability.<sup>50</sup> The SD is calculated using the following equation:

$$SD = \sqrt{\frac{\sum(X - \bar{X})^2}{N-1}}$$

The coefficient of variation calculated as the within-person standard deviation and is expressed as a percentage of the within-person mean therefore providing a measure of its absolute variability.<sup>51</sup> It is a standardized measure, allowing comparison of several gait variables that are recorded in different units of measurement.<sup>29</sup> The CV is calculated using the following equation:

$$CV = \left(\frac{SD}{\bar{X}}\right) 100\%$$

Few studies have suggested using SD when variability is unrelated to the size of the measured mean value.<sup>52</sup> If variability is proportional to the size of the measured mean value, then

the CV is an appropriate measure of variability.<sup>53</sup> If CV is used when variability is unrelated to the size of the measured mean value; the CV ratio may tend towards being inversely proportional to the within-subject mean value and may overestimate gait variability.<sup>47</sup> Consequently, in this dissertation we will calculate only SD to quantify gait variability.

Despite these reports, standards of quantifying gait variability were generally poor in the literature, with inadequate details to explain statistical aspects of gait variability measurement such as rationale for selection of CV or SD, and clarity regarding the use of individual or group mean/SD to calculate variability.<sup>6</sup>

### **2.1.5 Measurement methods of spatial and temporal gait variability**

Spatial and temporal gait characteristics can be measured by a variety of methods; instrumented computerized walkways,<sup>41,47,49</sup> footswitch systems,<sup>54,55</sup> triaxial accelerometer,<sup>56,57</sup> and gyroscopes with a Physilog datalogger<sup>58</sup> have all been used to measure and assess mean gait characteristics and variability. In this dissertation spatial and temporal gait characteristics were collected using a computerized walkway (GaitMat II) (EQ Inc, Chalfont, PA).<sup>37</sup>

The GaitMat II is an automated gait analysis system, based on the opening and closing of pressure sensitive switches on the walkway that are displayed on the computer screen as footprints when the participant walks (Figure 1 & 2). The GaitMat II provides a temporal resolution of 5 ms and a spatial resolution of 15 mm in both the longitudinal and transverse directions. The reliability and validity of the computerized walkway has been established for quantification of the spatial and temporal mean gait characteristics for a variety of populations

including children,<sup>59</sup> healthy young adults,<sup>60</sup> healthy older adults,<sup>7,60</sup> and individuals with Parkinson's disease<sup>61</sup> and Huntington disease.<sup>62</sup>



**Figure 1. Instrumented computerized walkway (GaitMat II)**

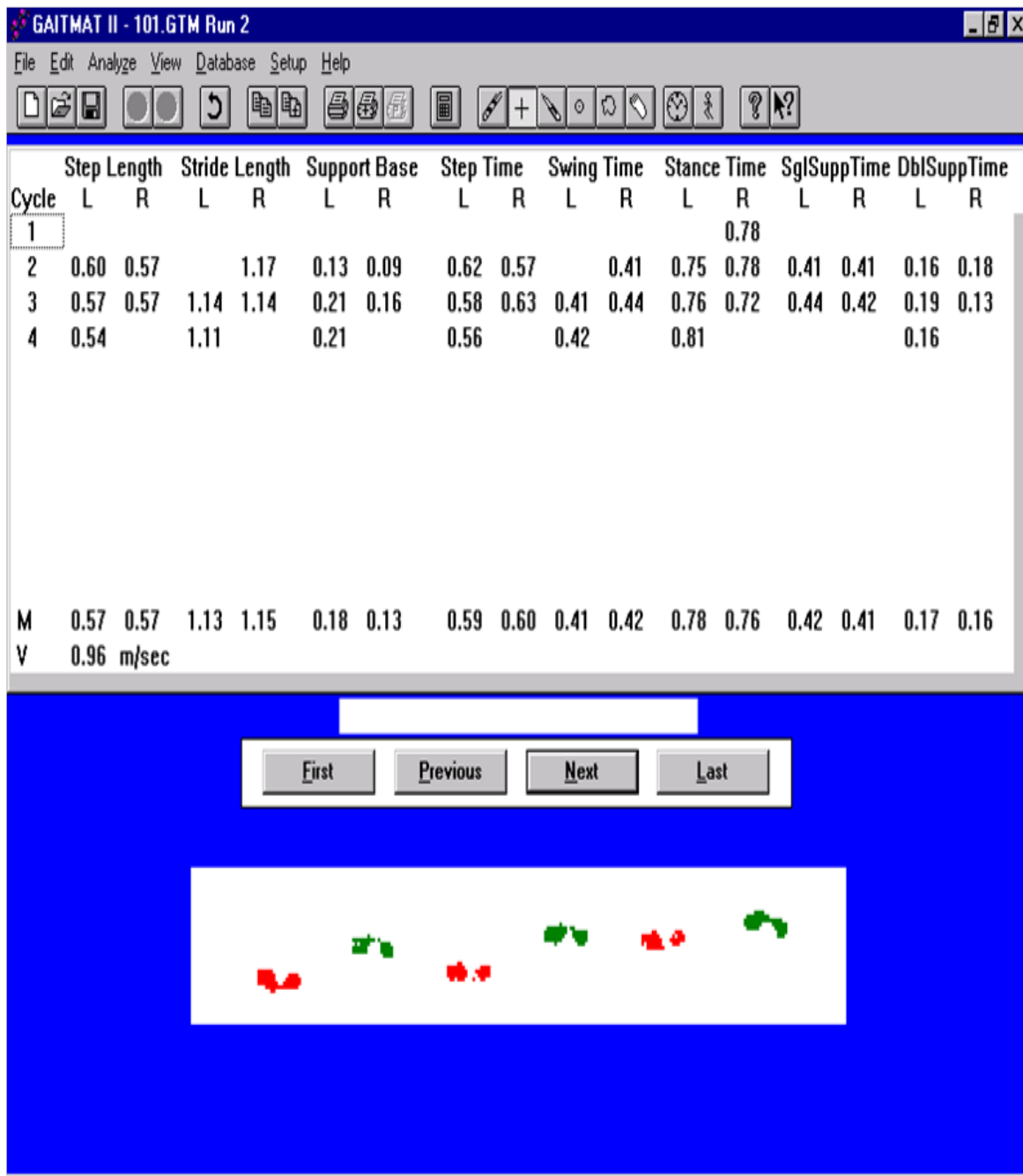


Figure 2. Real-time display during data collection (GaitMat II)

### **2.1.6 Clinical significance of spatial and temporal characteristics of gait variability**

Spatial and temporal characteristic of gait variability may discriminate important clinical features and has been used to quantify fall risk, to evaluate mobility, to assess risk of dementia, and to examine executive functioning in older adults.<sup>25,63-65</sup> Studies examined the clinical utility of gait variability included variability in stride speed,<sup>24</sup> stride time,<sup>64</sup> stride length,<sup>63</sup> step time, step length,<sup>44</sup> swing time<sup>66</sup> and step width.<sup>30</sup>

Measures of gait variability might provide additional insight into the neuromotor control of walking, assist in identifying gait instability and fall risk in older adults.<sup>32,64</sup> Gait variability data is thought to be a more sensitive predictor of falls than gait speed.<sup>28,48</sup> For instance, Brach and colleagues (2005) examined the relationship between gait variability and fall history in a population-based sample of more than 500 older adults, who did not walk slowly (i.e. gait speed  $\geq 1.0$  m/s). Too much or too little step width variability was associated with a fall history, while healthy values were positioned in the middle. Also, gait variability has been shown to be an independent predictor of future falls.<sup>25,28</sup> Some studies have shown that the magnitude of gait variability is altered in older adults who have history of falls compared to older adults who have not fallen.<sup>23,30,67</sup> Recently, gait variability has been used as a primary outcome measure in randomized controlled trials of intervention for falls prevention, including cognitive enhancers and multitask exercise program performed to the rhythm of piano music.<sup>68,69</sup> Consequently, measures of spatial and temporal gait variability may serve as a sensitive marker of unsteadiness and fall risk in older adults and a clinically relevant parameter in the response to therapeutic interventions.<sup>1</sup>

Gait variability is as an important indicator of impaired mobility in community-dwelling older adults and discriminates between older adults with and without mobility disability. High variability in temporal parameters of gait in relatively healthy older adults is associated with future mobility decline during a 5-year follow-up.<sup>31</sup> In addition, greater gait variability has been related to less confidence in walking and lower levels of daily physical activity in older adults.<sup>41</sup>

Gait variability is a more sensitive measure of subclinical pathology and aging than mean gait measures.<sup>25,26,30,70</sup> Gait variability is increased in individual with basal ganglia disorders, such as Parkinson's disease (PD) and Huntington's disease.<sup>71</sup> Increased gait variability can be seen throughout the different stages of Parkinson's disease (PD), even in patients who were only recently diagnosed with PD and have not yet started to take anti-Parkinsonian medications. The magnitude of gait variability tends to increase as the severity of disease increases.<sup>72</sup> Furthermore, in the "off" state, individuals with PD demonstrated increased stride time variability that could not be explained by Parkinsonian features such as tremor, rigidity, or bradykinesia. Increases in gait variability are also associated with degenerative neurological disorders such as Multiple Sclerosis, Alzheimer's, and amyotrophic lateral sclerosis.<sup>27,73,74</sup>

Increased gait variability is associated with increased cognitive requirements.<sup>67,75-77</sup> Gait variability predicts future cognitive decline<sup>63</sup> and discriminates between older adults with and without cognitive impairment.<sup>78</sup> In addition, Zimmerman et al. showed that higher gait variability was associated with lower levels of brain metabolism specifically in the hippocampus.<sup>79</sup>

Although clinical studies have focused on gait variability as an indicator of instability, falls, and cognitive decline in older adults, we know that not all alterations in gait variability are a marker of poor locomotor control. Natural variability in gait has been implicated as a protective

mechanism to prevent injuries during running by overcoming repetitive impact forces<sup>80</sup> and a key element for energy efficient and stable gait.<sup>81</sup> Also, in daily life when people are exposed to many challenges during walking including slippery surfaces, obstacles in the side walk, uneven terrain, etc., increased gait variability is needed to be able to adapt to these specific environmental conditions.<sup>82</sup>

### **2.1.7 Spatial and temporal characteristics of gait variability may represent different aspects of gait**

Different spatial and temporal characteristics are used to describe gait variability.<sup>83</sup> Variability of temporal characteristics such as step time, stance time and double support time, and spatial characteristics such as step length and step width may provide independent information of locomotion and should not be considered equivalent descriptors of gait variability. Instead, the specific gait characteristic should be specified, since increases in variability of a specific gait characteristic could be an indication of potential underlying mechanisms of the abnormal gait.<sup>40</sup> However, the rationale for choosing one specific gait characteristic in gait variability studies is not always clear or reported.

Over two decades ago, Gabell and Nayak (1984) hypothesized that gait characteristics represent two broad mechanisms of gait: step length and stride time represent gait timing mechanisms (i.e. pattern generator for gait), and step width and double support time represent postural control mechanisms.<sup>21</sup> Therefore, increase in step length or stride time variability could indicate a failure of the automatic stepping mechanism and increase in step width or double support variability may indicate a disruption in balance control. Recent evidence supports the theory of two broad mechanisms of gait and suggests different measures of gait variability may

represent different aspects of locomotor control such as adaptability and impaired balance control.<sup>47</sup> Investigators have suggested a higher degree of variability in stride length and time could possibly indicate a disturbance of the automatic stepping mechanism and therefore are more reliant on higher cortical levels of control in gait regulation more than musculoskeletal performance.<sup>21,84</sup> On the other hand, low variability values of stride time while steady-state walking, which reflect the automated rhythmic feature of gait, are indicators of safe gait and are used as a clinical index of gait stability.<sup>71,84</sup> Brach and colleagues reported decreased step width variability was related to sensory impairment which may contribute to balance deficits during walking, while increased stance time variability was related to central nervous system impairment.<sup>30,40</sup>

Martin et al. found associations between executive function-attention demand and processing speed for temporal, but not spatial, gait variability measures.<sup>42</sup> This is consistent with previous findings in younger people of increasing stride time variability, but not stride length variability, under dual-task cognitive interference.<sup>85</sup> Thus suggesting that stronger associations between executive function/attention and temporal versus spatial variability measures may be due to the timing component of the cognitive tests.<sup>86</sup>

If underlying mechanisms of gait variability are better understood, then distinct interventions may be designed to address specific deficiencies. Preventive and therapeutic interventions could target the underlying impairments. Patients with increased stance time variability may respond to a different therapeutic exercise program than those with increased step width variability. It is possible that individually designed therapeutic exercise programs based on the type of gait variability could result in greater improvements in walking function and overall mobility.<sup>40</sup>



### **2.1.8 Neural origins of gait variability**

The origins of variability in the spatial and temporal gait characteristics are uncertain. Variability of spatial and temporal parameters likely reflects disruptions in intrinsic motor or postural control during walking resulting from age- or disease-related decline in the central (brain, brainstem, and cerebellum) and peripheral nervous systems (muscles, joints).<sup>87,88</sup> Studies have shown increased gait variability with natural aging of the locomotor system,<sup>89</sup> different central nervous system disorders,<sup>27,73,87</sup> sensory loss,<sup>90</sup> lumbar spinal stenosis,<sup>91</sup> peripheral arterial disease (strength and range of motion deficits),<sup>64</sup> altered muscle activation pattern,<sup>92</sup> increased cognitive requirements,<sup>24</sup> and balance deficits.<sup>93</sup>

## **2.2 GAIT VARIABILITY AND AGING**

### **2.2.1 Preamble**

Human gait is an automated rhythmic motor task that involves the integration of multiple systems within the body (e.g. motor, perceptual and cognitive process).<sup>94</sup> During walking, automaticity and rhythmicity indicate a stable system able to reproduce similar limb coordinated movements from step-to-step while steady state walking. Gait instability is common in many older adults, even in absence of pathology.<sup>88</sup> Also, higher levels of variability during walking have been observed in older adults, as well as individuals that are at increased risk of falling.<sup>95</sup> Extreme levels of variability during walking both high and low might indicate motor-related pathologies.<sup>30,87,96</sup>

The focus of the following section is to describe gait characteristics in older adults and how they differ compared to younger adults, provide some examples of the magnitude of the mean spatial and temporal parameters for older and younger adults, and age-related changes in gait variability.

### **2.2.2 Gait Pattern in older adults**

It is well known in the clinical and epidemiological literature that gait changes with aging.<sup>97</sup> There are several differences in the spatial and temporal gait characteristics of older and younger people. Most investigators have found older adults walk slower, have a shorter step length, shorter relative swing phase time, and a wider step width. These age-related gait changes commonly associated with reduction in physical activity and in an increase number of falls or fall risk.<sup>97,98</sup>

The most commonly reported spatial and temporal alteration in the gait pattern of older adults is reduced gait speed.<sup>99</sup> For instance, Himann et al. reported that gait speed decreases 12–16% per decade after the age of 70.<sup>100</sup> Other studies have reported reductions in gait speed ranging between 0.03 m/s and 0.275 m/s for older adults.<sup>101</sup> Gait speed has been recommended as a “vital sign” for physical performance in older persons<sup>102,103</sup> and a 0.1 m/s decrease in gait speed is associated with higher falls risk in older persons.<sup>104</sup> Therefore, it is important that researchers and clinicians understand average values for gait speed in older adults. The comfortable gait speed value for healthy women aged between 70 and 79 years is 1.13 m/s and for men 1.26 m/s. In addition, a slower gait speed (mean 0.97 m/s) for community-dwelling older adults considered as transitioning to frailty.<sup>105</sup> A recent systematic review proposing a gait speed

of 0.8 m/s as a predictor of poor clinical outcomes and 0.6 m/s as a threshold to predict further functional decline in those older adults already impaired.<sup>106</sup>

Similar to the findings on gait speed, age-related reduction in stride length is commonly reported in the literature.<sup>98,107</sup> Reductions in stride length range from 0.03 to 0.14 m for male older adults<sup>108,109</sup> whereas, for female older adults they range from 0.076 to 0.34 m.<sup>110,111</sup> Changes with age in spatial and temporal parameter other than gait speed and stride length are inconsistent. For instance, some studies have reported an increase in stride time with age,<sup>112</sup> while others reported no change.<sup>107</sup> Similarly, some studies have reported a slight decrease in base of support with age,<sup>108,111</sup> whereas others report a slight increase in base of support.<sup>60,101</sup>

### **2.2.3 Age-related change in gait variability**

Walking is one of the most repetitive and “hard wired” human movements, so generally stride to stride fluctuation in most parameters of gait has been found to be small. In healthy younger adults, CVs of less than 3% have been reported for many of the spatial and temporal gait parameters such as gait speed,<sup>113</sup> stride time,<sup>21,75,84</sup> and step length.<sup>114,115</sup> In the same way, SD values for healthy young adults under normal conditions are less than 0.025 m for step width, less than 0.016 m for step length, and less than 0.032 s for stride time.<sup>44,48,49,116</sup> These small stride to stride fluctuations in spatial and temporal gait characteristics may reflect the inherent stability and consistency of neuromotor mechanism underlying normal walking.<sup>1</sup>

Variability of some of gait parameters increases with age.<sup>92,117</sup> Interestingly, the majority of studies have shown age-related gait variability changes are not statistically significant. Gabell and Nayak (1984), one of the earliest studies examining the effect of age on gait variability,

reported that CVs for step length, stride time, stride width and double support time were not significantly different between older and younger adults.<sup>21</sup> Other investigators have also reported similar values of gait variability between healthy younger and older adults for stride time, stance time, swing time,<sup>48</sup> step time, step length,<sup>116</sup> stride length<sup>111</sup> and step width.<sup>92</sup> These small values of gait variability reported for older adults may indicate that healthy aging might not alter neuromechanisms responsible for control of spatial and temporal parameters of gait on a step to step basis.

On the other hand, there have been a small number of studies reporting age-related alteration in the stride to stride fluctuations of some gait parameters. Kang and Dingwell (2008) reported significant difference in the variability of stride time ( $p = 0.018$ ), and step length ( $p = 0.005$ ), at all different walking speeds between older and younger adults.<sup>92</sup> Garbiner and colleagues (2001) found significant difference ( $p < 0.05$ ) in the variability of stride width, stride time and step length.<sup>118</sup> Owings and Garbiner (2004) also reported significant increases in step width ( $p = 0.037$ ) in older adults compared to younger adults.<sup>44,116</sup> A study by Callisaya et al. found that even within the older adult population (aged 60–86 years), increased gait variability was shown to be associated with advancing age in all gait measures ( $p < 0.05$ ) independent of height, weight and self-reported chronic disease.<sup>117</sup>

A possible reason for the ambiguous findings of the previous studies may lie in walking protocol employed to collect data affect gait variability data. Interestingly, studies which reported age-related changes in gait variability used treadmill,<sup>44,116</sup> while the majority of studies which reported no age-related changes in gait variability employed over-ground walking protocols.<sup>21,48</sup> Consequently, it is uncertain if age-related changes in gait variability reported by studies using treadmill compared to over-ground are due to the testing protocol employed to

collect gait data or to intrinsic differences between younger and older populations. Also, it is possible that the samples studied explain the difference between research studies, for example heterogeneity of walking ability and physical activity in older adults.

## **2.3 RELIABILITY OF GAIT VARIABILITY**

### **2.3.1 Preamble**

Gait variability has recently gained much attention in research and clinical studies.<sup>7,41,117</sup> Gait variability and its alterations are increasingly reported as a marker of gait performance and future mobility status in older adults.<sup>6</sup> However, reliability of variability of spatial and temporal of gait characteristics is not well established; unlike routine spatio-temporal parameters and gait speed which have been extensively evaluated for reliability.<sup>6,7,47,119,120</sup>

The knowledge of reliability data is a fundamental requirement in any gait analyses system. It enables us to decide whether any observed changes in an individual, i.e. due to exercise interventions or the normal aging process, are real changes, or are likely due to random or systemic error in the measurement technique. Similarly, the reported reliability data can be directly used to estimate the required sample size to uncover meaningful intervention effects.<sup>51</sup>

Reliability is defined as the consistency of a measurement tool or of an individual's test performance. Some amount of error is always present when testing human beings and, thus, reliability can be considered as the amount of error which is accepted for a particular test.<sup>121</sup> Baumgartner (1989) identified two types of reliability: relative and absolute.<sup>122</sup> Relative reliability is the degree to which individuals maintain their test result, or rank, or position within a group

over repeated measurements. This type of reliability is usually assessed with some type of correlation coefficient. Absolute reliability is the degree to which repeated measurements vary for individuals. This type of reliability is expressed either in the actual units of measurement or as a proportion of the measured values (dimensionless ratio).<sup>122</sup> Relative reliability statistics such as Intra-class correlation coefficients (ICCs) are affected by sample heterogeneity. For instance, a high ICCs may be obtained in situations where there is a large range of values in the sample and it does not necessarily mean that a test has acceptable reliability.<sup>60</sup> In contrast, absolute reliability statistics such as limits of agreement (LoA) are unaffected by sample heterogeneity and are more sensitive to changes in the participant's results over repeated tests.<sup>51</sup> In this investigation we will consider both types of reliability. By reporting each measure, an understanding of changes in both position and participant variation between tests is gained.

The following section reviews the reliability of spatial and temporal mean gait characteristics, and the reliability of spatial and temporal characteristics of gait variability.

### **2.3.2 Reliability of spatial and temporal mean gait characteristic and gait speed**

Test-retest reliability is an important quality of any gait measure, and it needs to be determined in order to differentiate between real changes in walking and biological variability.<sup>7,56</sup> Generally, gait speed and mean gait characteristics demonstrate high test-retest reliability in healthy older and younger adults with only exception for step width reliability. Low test-retest reliability for step width has been reported previously in healthy adults and has been attributed to the inherent variability of the parameter.<sup>60,123</sup>

In healthy subjects aged 21–71 years, high Intra-class correlation coefficients (ICCs) have been reported for gait speed, cadence and stride length (ICCs between 0.92 and 0.97) in normal and fast-walking, and moderate ICCs in slow-walking (ICCs between 0.78 and 0.91) obtained from three repeated trials recorded on one day.<sup>124</sup> Similarly, Menz et al. reported excellent test-retest reliability for walking speed, cadence and step length with (ICCs between 0.82 and 0.91) in older adults aged 76–87 years and younger adults aged 22–40 years recorded on two separate occasions, approximately 2 weeks apart.<sup>60</sup> Another study found high test-retest reliability for step length, step time and stance time with (ICCs ranging from 0.84 to 0.95) for young and older women over 2 separate test sessions.<sup>125</sup>

Furthermore, studies which examined reliability only in older adults have also reported high test-retest reliability for mean gait characteristics and gait speed. For instance, Hartman and colleague reported high ICCs for cadence, step duration, step length and walking speed (0.86–0.99) in older subjects aged 73.4 years.<sup>56</sup> Similar findings were reported for walking speed with ICCs between 0.84 and 0.93 in older adults with a mean age of 73.8 years.<sup>123</sup> A more recent study demonstrated high test-retest reliability ( $ICC \geq 0.86$ ) for most of the spatial and temporal gait parameters in healthy community-dwelling seniors during treadmill walking.<sup>119</sup>

### **2.3.3 Reliability of spatial and temporal characteristic of gait variability**

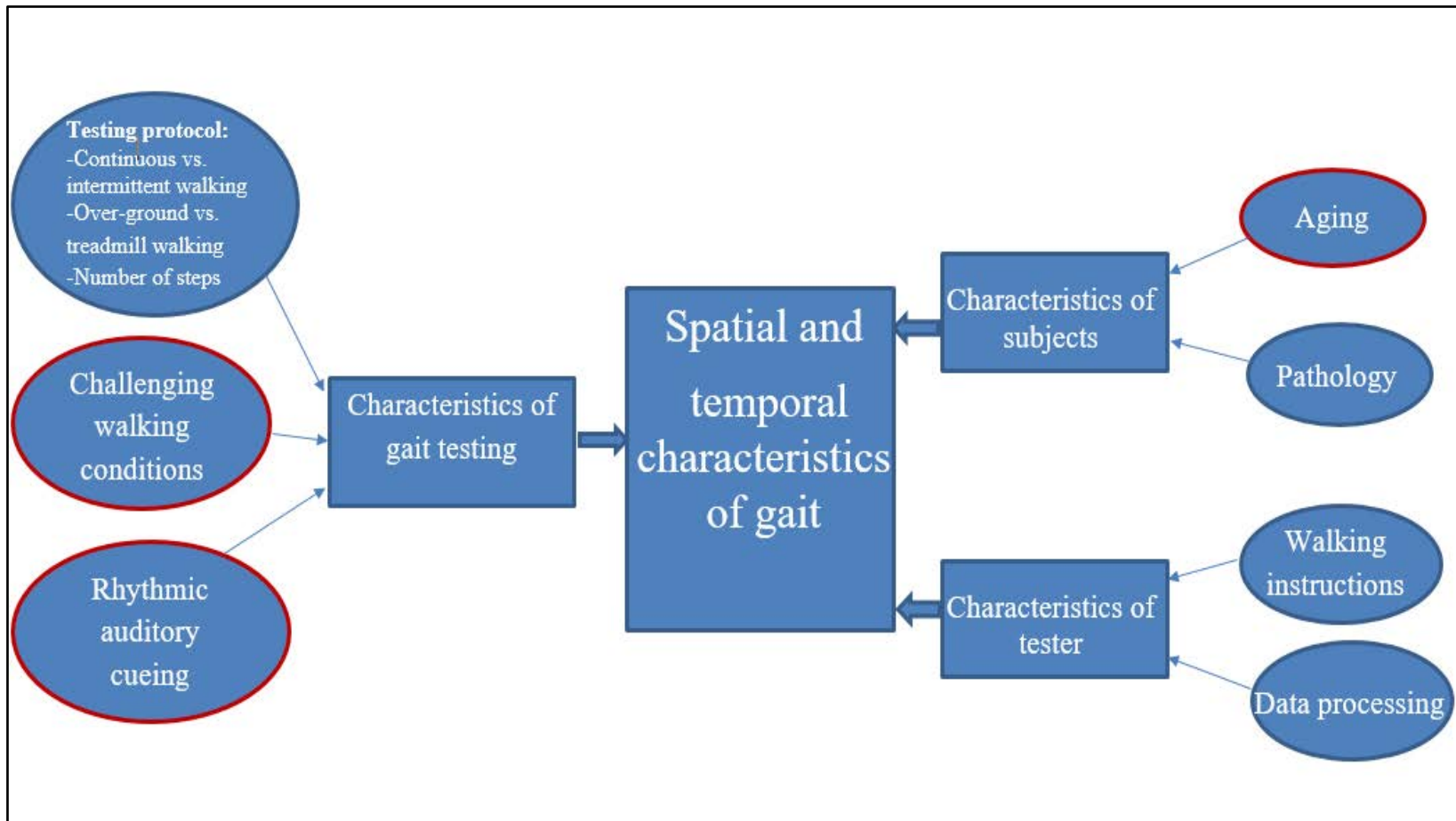
Although gait variability has been recently considered a more sensitive measure to assess gait performance in older adults than routine spatiotemporal parameters alone, there are few studies investigating test-retest reliability of gait variability measures in older adults.<sup>6</sup> Some studies found that test-retest reliability of gait variability measures to be lower than test-retest reliability

of mean gait characteristics. For example, Brach et al. observed considerably lower ICCs for spatio-temporal gait variability as compared to routine spatio-temporal parameters during over-ground walking.<sup>7</sup> Similarly, Faude et al. recently reported low reliability of gait variability parameters compared to spatio-temporal gait parameters during treadmill walking.<sup>119</sup> Furthermore, a recent systemic review of psychometric properties of gait variability in older adults reported that reliability results of gait variability are inconsistent; ranged from poor to excellent, with Intra-class correlations (ICCs) ranging from .11 to .98 depending on the variables reported.<sup>6</sup>

It is possible that the conflicting findings of estimate of gait variability are influenced by aging and pathology, the effect of a diverse range of walking protocols; uncertainty about the number of steps required for optimal measurement. As well as the wide range of variability outcomes described with no agreement for robust estimates on reliability. In light of the inconsistent findings of these studies, test-retest reliability of gait variability is currently unclear. Lack of knowledge of the reliability of gait variability measures limits the interpretation of gait variability from evaluative, diagnostic and prognostic studies.<sup>6</sup>

As such, it is necessary to review the different factors that have the potential to influence the estimate of spatial and temporal characteristics of gait in order to guide the use of spatial and temporal gait variability as an outcome measure in research and clinical studies. In the following section we propose a model that incorporates different intrinsic and extrinsic factors which may affect the estimate of spatial and temporal characteristics of gait: characteristics of gait testing protocol, characteristics subject, characteristics of tester as depicted in Fig. 3.





**Figure 3. A propose model outlines different factors which may affect spatial and temporal characteristics of gait.**

## **2.4 FACTORS MAY AFFECT THE ESTIMATE OF SPATIAL AND TEMPORAL CHARACTERISTICS OF GAIT**

### **2.4.1 Characteristics of subject**

#### **2.4.1.1 Aging**

Studies examined reliability of gait variability mainly in community dwelling older adults with a mean group age in the 8th decade. Reliability estimates of gait variability in healthy older adults varied depending on the variables reported, but were mostly fair to moderate. Table 2 below presents summary and findings from these studies.

The low reliability of gait variability in older adults requires a careful interpretation. It may be partly explained by age-related alterations in the step to step fluctuation of some gait parameters as outlined in chapter 2.2.3. The low reliability of gait variability may also be influenced by heterogeneity of walking abilities in older adults. Although participants in studies which reported reliability of gait variability were healthy active older adults, it is possible that these studies were comprised of older adults with some mobility limitations. For example, Brach et al. study included a relatively large sample of diverse community-dwelling older adults (N = 558); approximately (18%) of participants reported having fallen in the previous year and nearly (7.6 %) of sample reported using a cane during ambulation.<sup>7</sup> Similarly, in Hartman et al. study about (39%) of participants reported at least 1 fall during the last half year; and the activity level of participants varied from sedentary to regular exercise behavior.<sup>56</sup>

Furthermore, it is possible that the older adult's fluctuations in gait overtime may strongly affect the reliability of gait variability. For example, Hartman et al. reported the interrater reliability (assessed by two different raters with 20 minutes apart) was slightly better results compared to intrarater reliability (assessed by one rater only with 5-10 days apart).<sup>56</sup> Similarly, Faude et al. (2012) reported within-day reliability (same day with 30 minutes apart) was higher compared to between-day reliability (three times with weekly interval) for gait variability.<sup>119</sup> Consequently, it is possible that underlying subclinical pathology in important neural locomotor regions in older adults might contribute to inconsistent walking overtime and low reliability estimates.

To date, the effect of age upon reliability of gait variability has not been investigated. As such, an examination of reliability of gait variability in healthy younger adults is necessary. Therefore, study 1 of this dissertation will compare test-retest reliability of spatial and temporal characteristics of gait variability in healthy younger and older adults.

**Table 2. Summary of studies reporting reliability of gait variability in healthy older adults.**

Study	Sample	Instrument	Walking trial characteristics	Number of steps/strides	Results
<b>Brach et al. (2008)</b>	558 older adults (339 females; 219 males, mean age 79.4)	4 m GaitMat II (plus initial and final 1 m inactive sections to allow for acceleration and deceleration of the participant).	Participants completed 2 practice passes on the GaitMat II followed by 4 passes at their self-selected walking speed for data collection (1 pass for the 4-m analyses and 2 passes for the two, 4m analyses)	5–6 steps from single 4 m walk and 10–12 steps from two, 4 m walks	Single 4-m walk, showed poor reliability for step width and stance time variability (ICC = 0.22 and 0.37, respectively) and fair reliability for step length variability (ICC = 0.48).  Two, 4-m walks showed fair to good reliability for step width, stance time and step length variability (ICC = 0.40, 0.63, 0.50 respectively)
<b>Faude et al. (2012)</b>	20 older adults (10 females, 10 males, mean age 64.8), with no known health impairments (e.g. orthopedic, neurological, or internal diseases).	One-dimensional ground reaction force measuring treadmill.	Between-day variability (three days within weekly interval) and within-variability of temporal and spatial gait parameters examined on a treadmill walking. Subjects walked at their comfortable walking speed on a treadmill after a short familiarization period of 1 minute.	400 steps	Between-days variability showed fair reliability for stride time (ICC = 0.44) and poor reliability for stride length (ICC = 0.22). Within-day variability showed fair to good reliability for stride time and stride length (ICC = 0.72, 0.74 respectively)
<b>Hartmann et al. (2009)</b>	23 older adults, independent living (15 females, 8 males, mean age 73.4 years) able to walk without an aid	The DynaPort <sup>MiniMod</sup> tri-axial accelerometer	Between session testing, subjects walked at preferred gait speed over 24 m walk (18m assessed) in four conditions; gym floor, gym floor dual task, rubber walkway, rubber walkway dual task. Repeated 3 times, once on first occasion and twice 5–10 days later (20 min apart).	Not reported	ICCs of gait variability ranged from 0.12 to 0.88 for step duration and step length.

Table 2 (continued)

<b>Hollman et al. (2010)</b>	24 older adults (11 females, 13 males, age ranged from 67 to 87 years)	5.6 m GAITRite (plus 2m acceleration and deceleration)	Within session testing subjects walked during normal and dual task (backward spelling), three times for each walking conditions at self-selected speeds.	13 strides in normal walking, 14 strides dual task walking.	Test–retest reliability for variability in stride velocity was fair to good (ICC = 0.656) in normal walking and poor (ICC = 0.226) in dual task walking.
<b>Moe-Nilssen et al. (2010)</b>	23 older adults (15 females and 8 males, mean age 80 years)	4.88m GAITRite (plus 2 m acceleration and deceleration)	Within session testing. 2 trials at preferred speed, repeated after a short rest. 2 trials at slow, preferred and fast speeds. Gait parameters were selected for subsequent construct validity analysis from test-retest reliability results (if ICC $\geq$ 0.80)	Average 34.5 in four walks	Test–retest reliability showed excellent reliability for step time and step length (ICC = 0.83, 0.81 respectively); fair to good reliability for stride time, stride length and single support time (ICC= 0.64, 0.50, 0.68 respectively); and poor reliability for step width and stride velocity (ICC= 0.22, 0.11 respectively)
<b>Najafi et al. (2009)</b>	27 older adults (18 females and 9 males, mean age of 80.3 years)	(i) Body worn sensors (gyroscopes) and Physilog datalogger (ii) 6.25 m GAITRite™ (plus 2 m acceleration and deceleration)	Within session testing. Test–retest reliability calculated from 5m GAITRite walk and 20m Physilog system walk. Both walked at preferred speeds, repeated after 15min rest	Not reported	Test–retest reliability for gait cycle time was fair (ICC= 0.42), by 5 m GAITRite™ and 5 m Physilog and poor (ICC= 0.10) by 20 m Physilog. Test–retest reliability for stride velocity was fair to moderate (ICC = 0.37) by 5 m GAITRite™, and 5 m Physilog, (ICC= 0.50) 20 m Physilog

### 2.4.1.2 Pathology

Step to step fluctuation of walking has been shown to be altered in some neurologic conditions such as Parkinson's disease (PD), Huntington disease,<sup>71</sup> Alzheimer's disease,<sup>27</sup> as well as in cognitive decline.<sup>126</sup> Gait variability measures may provide a sensitive marker of the neuromotor performance reflective of additional insights of impaired walking, beyond those commonly characterized using average gait values.<sup>25,30,32</sup> However, few studies explored the effect of pathology on reliability of gait variability. Table 3 below summarizes the findings of studies investigating reliability of gait variability in some clinical populations such as patients with Dementia and PD.

Few studies have investigated the reproducibility of gait variability measures in people with dementia, and the results were inconsistent. A study of older adults with frontotemporal degeneration and dementia reported slight to poor reliability ( $ICC < 0.20$ ) for stride time variability between two trials within the same session.<sup>127</sup> In contrast, a study of spatial and temporal gait variability in a group of hospital-in patients with dementia of unspecified sub-type, reported a moderate to excellent reliability for stride length and stride time variability ( $ICC = 0.88, 0.56$  respectively) over two weeks.<sup>123</sup> A recent study investigated reproducibility of spatial and temporal gait variability measures of people with mild to moderate Alzheimer's disease on two occasions one week apart, reported poor to moderate reliability of gait variability obtained using 12 strides. Consequently, it is important to establish reproducibility of gait variability measures for each specific sub-type, as gait characteristics differs between different types of dementia.<sup>128</sup> Increased gait variability is commonly reported in individuals with basal ganglia disorders such as Parkinson's disease.<sup>71,129</sup> Hausdorff et al. provided evidence that alterations in

gait variability manifest relatively early in the disease process even though dramatic changes in speed may not yet be apparent.<sup>71</sup> Recent research also suggested that gait variability has the potential utility as a predictive measure of dysfunction in Parkinson's disease (PD).<sup>6</sup> However, to date only one study has explored the reliability of gait variability measures in individuals with PD. Galna and colleagues (2013) examined reliability of gait variability in healthy older adults and individuals with PD on two occasions one week apart; surprisingly, they did not find significant differences between participants with PD and healthy older adults on reliability estimates. Their findings suggested that mild to moderate PD doesn't negatively impact reliability of gait variability; and gait fluctuations in more severe PD group may result in less reliable estimates of gait variability.<sup>120</sup>

#### **2.4.2 Characteristics of tester**

Reliability studies in gait reported some situations where tester or examiners can be a potential source of error that might influence reliability estimate.<sup>130,131</sup> For example, the instructions or amount of verbal encouragement may vary from one examiner to another or from one measurement session to the next. Also, the tester may have a tendency to report specific numbers rather than the actual measured values. The knowledge of the previous value may influence the examiner's perception of the current measured values. Additionally, the way the tester inspects and cleans the data from instrumented walkway such as GaitMat may vary from one person to another, which can affect reliability of gait variability. Consideration the effect of characteristics of tester on gait variability is beyond the scope of this thesis.

**Table 3. Summary of studies reporting reliability of gait variability in clinical population.**

Clinical population	Study	Sample	Instrument	Walking trial characteristics	Number of steps/strides	Results
<i>Dementia with Frontotemporal degeneration (FTD)</i>	Beauchet et al. (2009)	69 community-dwelling cognitively healthy older individuals (mean age $75.5 \pm 4.3$ ; 43.5% women) and 14 demented patients with FTD (mean age $65.7 \pm 9.8$ years; 6.7% women)	3.5 m GAITRite® (plus 2 m acceleration and deceleration) and 10 m SMTEC® footswitch systems	Each subject completed two trials at self-selected walking speed for all the testing conditions; single tasking and dual tasking (walking while counting backward (CB) aloud starting from 50	Not reported	ICC of stride time variability was slight to poor, in both groups while single and dual tasking conditions (ICC < 0.20), except while dual tasking in demented patients where ICC was fair (ICC = 0.34)
<i>Parkinson's disease (PD)</i>	Galana et al. (2013)	27 older adults (20 females and 7 males, mean age 72.2 years) and 25 participants with mild-to-moderate PD (12 females and 13 males, mean age 68.1 years)	7 m GAITRite	Gait variability was measured twice, one week apart, under two different conditions at their preferred walking speed (i) continuous (ii) intermittent walks. The continuous walks involved walking for 2 min around a 25 m oval circuit. The intermittent walks, involved three walking trials 12 m	Median of 29 steps for intermittent walks 57 steps during continuous walks	Reliability of gait variability ranged from poor to excellent (ICC = .041–.860); Gait variability was more reliable during continuous walks.
<i>Dementia</i>	Van Iersel et al. (2007)	85 patients participated (47 females, 38 males, mean age 75.8 years). 39 patients were diagnosed with mild or moderate dementia and 46 participants without dementia.	5.6 m GAITRite	Between session testing, participants walked over mat at preferred speed. Clinical change in gait determined by video gait analysis (N = 3 experts); rated as stable or relevant change (non-stable) over 2-week period.	Not reported	Reliability of gait variability was moderate to high. Test-retest reliability, for individuals with dementia stride time (ICC=0.56), stride length (ICC= 0.88); individuals with no dementia stride time (ICC = 0.84), stride length (ICC = 0.88).



Table 3 (continued)

	Van Iersel et al. (2008)	Same cohort as above, participants classified according to stability of gait performance, 59 were stable; and 26 showed a clinically relevant change in gait.	5.6 m GAITRite	Between sessions testing; same protocol as above. For overall stride time and for stable patients (stride time only).	Not reported	Test-retest reliability high for all variables (ICC= 0.82 to 0.98) apart from overall stride time (ICC= 0.46), which increased to (ICC = 0.72) when stable patients only were assessed.
<i>Alzheimer's disease</i>	Wittwer et al. (2013b)	16 community dwelling older adults with mild to moderate Alzheimer's disease (mean age 80.1 years)	Instrumented mat	Participants walked at self- selected speed, two familiarization walks were followed by 12 trials	12 strides	Inclusion of 12 strides/steps (12-VM) yielded moderate reliability for the spatial variability measures of stride length and width (ICC=0.60, 0.75 respectively) and poor reliability for velocity and cadence variability (ICC=0.27, 0.07 respectively).

### **2.4.3 Characteristics of gait testing protocol**

#### **2.4.3.1 Over-ground versus treadmill walking**

Studies investigating gait variability in younger and older adults have employed different gait testing protocols. The main difference between these studies lies in the use of either a treadmill<sup>44,132,133</sup> or over-ground walking protocol.<sup>21,30,48</sup> The use of treadmill among researchers is favored due to space limitation, the ability to control speed, the ease of use in collecting the required number of steps to analyze gait variability data and the incorporation of safety feature such as harnesses.<sup>134,135</sup> Despite these benefits, there have been suggestions that the imposed constant speed of a treadmill may artificially impede the natural variation that occurs during over-ground walking. Studies have shown that gait parameters including gait variability are altered during treadmill walking.<sup>116,133</sup> For example, Dingwell et al. (2001) reported that stride time variability is significantly reduced in treadmill compared to over-ground walking in older adults.<sup>132</sup> Also, metabolic cost has been reported to be higher during treadmill walking when compared to over-ground walking in healthy older adults.<sup>135</sup> Additionally, treadmill walking may be foreign or new to the older adults. A previous study reported that older adults require greater than 15 minutes to familiarize to treadmill walking.<sup>136</sup> In healthy younger adults, step width variability is significantly decreased when walking on a treadmill compared to over-ground walking.<sup>137</sup>

Employing a treadmill might affect reliability of gait variability measure due to altered magnitude of gait variability and reduce natural walking variations that occur during over-ground walking. To date only one study has investigated the reliability of gait variability during

treadmill walking, and reported low reliability of spatial and temporal gait variability in healthy older adults.<sup>119</sup>

#### **2.4.3.2 Continuous versus intermittent over-ground walking**

Another existing issue to the influence of walking protocol upon the estimate of gait variability is whether to collect data during continuous or intermittent over-ground walking. Intermittent walking protocols generally involve repetitive periods of waiting, gait initiation in response to an auditory command, steady-state walking for several strides, followed by gait termination at the end of a short walkway. In contrast, continuous walking protocols typically involve walking without interruption over longer distances. A recent study investigated the effect of intermittent and continuous over-ground walking protocols upon measures of gait variability and reported higher gait variability with intermittent walking protocols compared to continuous walking.<sup>49</sup> Similarly, Galna et al. evaluated the effect of continuous over-ground walking to intermittent walks on reliability of gait variability and reported that continuous walking resulted in more reliable estimates.<sup>120</sup>

Continuous walking protocols may be more reliable because they measure gait under a steady state condition reflecting more automatic gait control unconfounded by the frequent disruptions to the temporal locomotor rhythm of gait experienced during short intermittent walks.<sup>49,120,132</sup> Although continuous walking demonstrated higher reliability compared to intermittent over-ground walking, Lord et al. argued that our daily walking largely occurs in short, interrupted bursts of walking and the distance walked during testing may reflect different

aspects of motor control (e.g. attention may play a greater role in short, interrupted walks), and rationale for selection needs to be explicit within the test protocol.<sup>6</sup>

#### **2.4.3.3 Number of steps/strides**

Another characteristic of walking testing protocol which may impact the estimate of gait variability is the number of steps/strides selected. Researchers have explored the number of steps/strides and distance required for optimal gait variability measurement.<sup>6</sup> Although the number of steps/strides to improve the reliability of gait variability is still uncertain, the overall findings from studies recommend collecting gait data over a reasonable distance. Hartmann et al. recommend a minimum of 20 meters or 25 steps for step duration and step length variability.<sup>56</sup> Brach et al. reported greater test-retest reliability of gait variability recorded from 10-12 steps compared to 5-6 steps.<sup>7</sup> In individuals with Alzheimer disease, Wittwer et al. reported the best reliability for velocity, stride length and cadence variability achieved by using an average of 64 strides.<sup>128</sup> Use of only 12 strides produced poor to moderate reliability so whilst this number may be sufficient for reliable measures of gait variability in people who are cognitively intact.<sup>6</sup> In a more recent work, Galna et al. recommended at least 30 steps to improve the reliability of gait variability although 50 steps or more is optimal.<sup>120</sup> In contrast, Hollman et al. recommend data from 370 strides to achieve ICC of 0.90 for gait velocity variability during intermittent walks in older adults.<sup>46</sup> Owings and Grabiner (2003) reported that more than 400 steps are needed to accurately estimate the gait variability of younger adults walking on treadmill.<sup>134</sup> However, recoding gait variability from hundreds of strides may be impractical number for older adult

population as they easily become fatigued. Patient burden must take into consideration, when selecting the number of steps/strides to be included in gait analysis.

Furthermore, studies which investigated reliability of gait variability reported both step and stride analysis to calculate gait variability, although the rationale for selecting one or the other, or both, was unclear. Moe-Nilssen et al. reported all stride variability measures demonstrated lower reliability than the equivalent step variability measures which can be explained by the fact that twice as many steps as strides were included for each individual.<sup>47</sup> Similar findings also reported by Galna et al. who found data from left and right steps combined was more reliable than using strides and suggested combining left and right step variability (calculated separately prior to combining) may also act to reduce the effect of outliers.<sup>120</sup>

#### **2.4.3.4 Gait speed**

The majority of studies investigated gait variability at preferred gait speed. Although it is known that minimal gait variability occurred near or close to the preferred walking speed,<sup>84,138,139</sup> where energy expenditure of walking are also minimal and head stability is maximal.<sup>140,141</sup> This pattern of optimization at preferred gait speed might be due to the inherent interaction of neural and biomechanical mechanisms, with only minimal active control of high-level sensory feedback control.<sup>142</sup>

Biomechanical analysis of gait mechanisms reveals a complex relation between gait speed and measures of gait variability. In younger adults, some studies demonstrated a quadratic relation between gait speed and gait variability with fixed walking speeds on a treadmill, where

variability increased at speeds slower or faster than preferred speed.<sup>114,143</sup> Similarly, Beauchet et al. reported a quadratic and statistically significant relation between decreased gait speed and increased gait variability in younger healthy adults during over-ground walking.<sup>144</sup> While other studies have failed to determine a relation between gait speed and gait variability.<sup>92,116</sup>

Studies investigating the effects of gait speed on gait variability in older adults provide inconsistent findings. Majority of previous studies examined the effects of gait speed on gait variability during over-ground walking, where subjects were directed to walk “slow,” “fast,” and “usual”. Although these walking protocols allow comparison between speeds, it is difficult to make comparisons between subjects since each subject walked at different speeds from other subjects.<sup>110,145,146</sup> To address this issue Kang and Dingwell (2008) examined gait variability in both younger and older adults across multiple controlled walking speeds using a treadmill. They reported gait variability in older adults was not affected by changes in walking speed more than younger adults and therefore age-related changes in variability were found independent from the influence of walking speeds.<sup>92</sup> Supporting this, a number of studies have shown associations between walking variability and falls but not between gait speed and falls in older adults.<sup>25,28,48,64</sup> Other studies investigating the effects of age on gait variability have shown no significant difference in gait variability between healthy younger and older adults, even though older adults walked at slower gait speed.<sup>21,48,118</sup>

In contrast, other studies have suggested that gait speed is a confounding factor for gait variability in older adults.<sup>145,147</sup> Similarly, Callysia et al. suggested age-related changes in temporal variability measures may be largely due to reduced walking speed, while spatial variability was less dependent on gait speed.<sup>117</sup> This finding is conflicting with previous studies which found stance time variability was independent predictor of mobility during a self-selected

walking speed.<sup>31</sup> Previous studies confirm that slow speed induces higher step time variability.<sup>114,144</sup> Slow walking speed also induces a specific spatial and temporal adaption (higher walk ratio) that was “un-natural” for many subjects, what induced greater variability.<sup>113</sup> Other studies reported high stance time variability at slow and fast speeds.<sup>144</sup> Recently, Beauchet et al. reported high stance time variability at fast-pace walking speed compared to usual pace in individuals with mild cognitive impairment.<sup>148</sup>

Although the speed-dependent nature of gait variability remains unclear, gait speed should be considered a potential confounding factor when examining gait variability. Consequently, study two of this dissertation will examine the impact of slower and faster speeds on spatial and temporal gait variability in younger and older adults.

#### **2.4.3.5 Rhythmic auditory cueing (metronome)**

External cueing is defined as providing discrete external sensory information, usually via rhythmic auditory or visual stimuli, which serve as a target or trigger for movement generation.

<sup>149</sup> The focus of this dissertation will be on rhythmic auditory cueing.

The synchronization of body movement to external auditory rhythm (auditory-motor coordination) is a remarkable capacity of the human brain.<sup>150,151</sup> A rhythmic auditory cue has been widely used to cue rhythmic movements such as walking,<sup>152</sup> and has gained popularity in gait rehabilitation because it exhibits positive effects on various spatial and temporal gait characteristics of patients with neurologic impairments, including stroke and Parkinson’s disease.<sup>15,149,153</sup>

Neural pathways that mediate auditory-motor synchronization are not yet fully understood; however, connections between auditory and motor regions are known to be extensive. Early studies identified that sound could facilitate muscle activation via the reticulospinal system.<sup>154</sup> A more recent functional magnetic resonance imaging study has shown the posterior superior temporal gyrus and premotor cortex to be key structures for entrainment of motor responses to external rhythms.<sup>155</sup> Other brain regions also implicated in rhythm synchronisation include supplementary and pre-supplementary motor areas, cerebellum and basal ganglia.<sup>155</sup>

Rhythmic auditory cues range in type from a simple rhythmic beat such as a metronome cue to specifically composed complex rhythmic music with accentuated beats. Hausdorff et al. investigated the influence of rhythmic auditory cues on spatial and temporal gait parameters and found no change in the gait velocity and stride length of healthy older adults with metronome cues matched to their baseline cadence.<sup>32</sup> Recently, Wittwer et al. also reported no change in the spatio-temporal mean value in healthy older adults with metronome cues delivered at the same frequency as their preferred speed cadence, but they walked faster in time to music cues.<sup>152</sup> Similar findings were reported in a group of healthy younger adults who walked faster in time to music than to metronome cues at a range of tempi, suggesting that the extra auditory elements in the music may have enhanced their motor performance more than simple beat cues.<sup>156</sup> In contrast, a metronome produced an increase in gait speed in a group with Huntington's disease (HD) and this increase was more pronounced with greater disease severity.<sup>157</sup>

Rhythmic auditory cueing including metronome may also affect gait variability. However, the majority of studies investigating the effects of a single rhythmic auditory cueing on temporal gait variability have reported inconsistent results.<sup>88,158</sup> It seems intuitive that



synchronizing movement to a rhythmic beat may reduce temporal gait variability; however, the process of synchronizing may increase executive function load which may have the opposite and undesirable effect of increasing gait variability.<sup>159</sup> In healthy groups metronome cues delivered at 10% below preferred speed cadence,<sup>158</sup> at usual step rate, and 10% higher<sup>88</sup> preferred speed cadence resulted in an increase in gait temporal variability. Increased temporal variability of gait was also reported in groups with Parkinson's disease at metronome cue frequencies of both 20 % below preferred speed cadence<sup>160</sup> and 10% higher preferred speed cadence<sup>88</sup> potentially supporting the proposal that metronome increase cognitive load. In contrast, two other studies of individuals with Parkinson's disease found that metronome cue frequencies at both 10% below preferred speed cadence<sup>158</sup> and at usual step rate<sup>161</sup> decreased gait temporal variability.

Few studies reported the effect of rhythmic cues on both spatial and temporal gait variability. For example, Thaut et al. (1993) examined effect of rhythmic music cues on gait spatio-temporal variability and reported decreased timing variability only in a group with stroke. A more recent study which investigated the effects of both rhythmic music and metronome cues on spatial and temporal gait variability in healthy older adults, reported the spatial and temporal gait variability did not increase with either music or metronome cues; thus suggesting the cues did not disrupt gait timing.<sup>152</sup> Conflicting findings may be due to the variety of gait parameters, testing protocols and analysis methods used as well as the effects of different populations and cue frequencies in these studies.

Consequently, study three of this dissertation will investigate the impact of metronome cues on the spatial and temporal coordination of gait at different walking speeds in healthy adults. Understanding the impact of rhythmic auditory cueing on the spatial and temporal

coordination in healthy adults in the absence of aging and pathology is an important first step in furthering our understanding of the neuromotor control of gait at different walking speeds.

### **3.0 THE TEST-RETEST RELIABILITY AND MINIMAL DETECTABLE CHANGE OF SPATIAL AND TEMPORAL GAIT VARIABILITY DURING USUAL OVER-GROUND WALKING FOR YOUNGER AND OLDER ADULTS**

**Background.** Gait variability is a marker of gait performance and future mobility status in older adults. Reliability of gait variability has been examined mainly in community dwelling older adults who are likely to fluctuate over time.

**Objective.** The purpose of this study was to compare test-retest reliability and determine minimal detectable change (MDC) of spatial and temporal gait variability in younger and older adults.

**Study design.** Repeated measures design.

**Methods.** Forty younger (mean age =  $26.6 \pm 6.0$  years) and 46 older adults (mean age =  $78.1 \pm 6.2$  years) were included in the study. Gait characteristics were measured twice, approximately 1 week apart, using a computerized walkway (GaitMat II). Participants completed 4 passes on the GaitMat II at their self-selected walking speed. Test-retest reliability was calculated using Intra-class correlation coefficients ( $ICCs_{(2,1)}$ ), 95% limits of agreement (95% LoA) in conjunction with Bland-Altman plots, relative limits of agreement (LoA%) and standard error of measurement (SEM). The MDC at 90% and 95% level were also calculated.

**Results.** ICCs of gait variability ranged 0.26-0.65 in younger and 0.28-0.74 in older adults. The LoA% and SEM were consistently higher (i.e. less reliable) for all gait variables in older compared to younger adults except SEM for step width. The MDC was consistently larger for all gait variables in older compared to younger adults except step width.

**Conclusion.** ICCs were of limited utility due to restricted ranges in younger adults. Based on absolute reliability measures and MDC, younger had greater test-retest reliability and smaller MDC of spatial and temporal gait variability compared to older adults.

**Key words.** Reliability, Gait, Variability, Younger, Older

### 3.1 INTRODUCTION

Gait variability is a quantifiable feature of walking defined as fluctuations in the spatial and temporal gait characteristics from one step or stride to the next.<sup>7,41,117</sup> Gait variability has recently gained much attention in research and clinical studies. Measures of gait variability might provide additional insights into the neuromotor control of walking, assist in identifying mobility dysfunction and fall risk in older adults, above and beyond mean values of gait parameters such as average gait speed or step time.<sup>6,30,31</sup> In this sense, measures of spatial and temporal gait variability are becoming important clinical tools.

Test-retest reliability is a fundamental psychometric requirement for any measure. However, the reliability of spatial and temporal gait variability is not well established.<sup>6,7,47,120</sup> The reliability of gait variability has mainly been examined in community dwelling older adults

with a mean group age in the 8th decade. The reliability of gait variability in older adults is inconsistent; ranging from poor to excellent, with intra-class correlation coefficients (ICCs) ranging from 0.11 to 0.98 depending on the variables reported.<sup>6,120</sup> Lack of knowledge of the reliability of gait variability measures limits the interpretation of gait variability from evaluative, diagnostic, prognostic and intervention studies.<sup>6,117</sup> In this regard, it is important to know the minimal detectable change (MDC) to support the use of gait variability as an outcome measure in clinical or research settings. The MDC allows investigators to determine if an observed change is a true change or simply a result of a measurement error.<sup>162</sup>

Healthy older adults exhibit greater variability in basic spatial and temporal measures of gait when compared to healthy young adults.<sup>44,116,163</sup> Gait variability is thought to be a function of the neurological integration of numerous sensory inputs (e.g., visual, auditory, vestibular, proprioceptive, etc.) and feedback processes that take place during the generation of each gait cycle.<sup>39</sup> An increase in gait variability is indicative of a decline in the coordination of the locomotor control system and its complex integration of interdependent components.<sup>28</sup> Older adults may fluctuate in their walking from hour to hour, day to day, week to week which could impact the reliability of gait variability whereas walking in younger adults is more stable (fluctuates less), thus potentially leading to more consistent measurements or greater test/retest reliability. In older adults, it is possible that underlying subclinical pathology in important neural locomotor regions might contribute to inconsistent walking over time and low reliability estimates.<sup>163</sup>

The purpose of this study was to (i) compare the test-retest reliability and (ii) determine the minimal detectable change (MDC) of spatial and temporal gait variability in younger and

older adults over one week. Younger adults are more stable and fluctuate less in their walking over time compared to older adults.<sup>163</sup> Therefore, we hypothesized that younger adults will have greater test-retest reliability and smaller MDC of spatial and temporal gait variability compared to older adults.

## **3.2 METHODS**

### **3.2.1 Participants**

Forty younger and 46 older adults were included in the study. The younger adults were recruited through fliers posted throughout the University of Pittsburgh. The younger participants were of age 18-50 years, ambulated independently, and had no diagnosed neuromuscular, cardiopulmonary, or orthopedic conditions that would affect walking. The younger participants were first screened over the phone to determine initial eligibility. Subjects who passed the phone screen were scheduled for a one hour clinic visit which included a physical exam (range of motion and muscle testing) to determine final eligibility followed by measurement of gait characteristics using a computerized walkway.

Older participants were identified from a prospective longitudinal study of gait and balance in older adults.<sup>164</sup> The inclusion criteria for the older adults were age 65 or older; self-reported ability to tolerate a five-hour session (with rest periods) of answering questionnaires and performing walking tests; ability to walk a household distances (approximately 50 ft) at a minimum, with or without an assistive device and without the assistance of another person. Also, the older adults had to be free of (a) neuromuscular disorders that impair movement

(including but not limited to Parkinson's disease, stroke, and multiple sclerosis); (b) cancer with active treatment (specifically radiation or chemotherapy) within the past 6 months; (c) non-elective hospitalization for a life-threatening illness or major surgical procedure in the past 6 months; (d) severe pulmonary disease requiring supplemental oxygen or resulting in difficulty breathing at rest or with minimal exertion (such as walking between rooms in their home); and (e) chest pain with activity or a cardiac event, such as heart attack within the past 6 months. The older participants were first screened over the phone to determine initial eligibility. Subjects who passed the phone screen were scheduled for a clinic visit which included a physical exam to determine final eligibility. Older adults completed 5 h of testing, including a measurement of gait characteristics which occurred within the first hour of testing. Both studies of younger and older adults were approved by the University of Pittsburgh Institutional Review Board, and all participants provided informed consent prior to participation.

### **3.2.2 Gait characteristics**

Spatial and temporal gait characteristics were collected using a computerized walkway (GaitMat II) (EQ Inc, Chalfont, PA).<sup>37</sup> The GaitMat II is an automated gait analysis system, based on the opening and closing of pressure sensitive switches on the walkway that are displayed on the computer screen as footprints when the participant walks. The GaitMat II provides a temporal resolution of 5 ms and a spatial resolution of 15 mm in both the longitudinal and transverse directions. The reliability and validity of the computerized walkway has been established for quantification of the spatial and temporal mean gait characteristics for a variety of populations

including children,<sup>59</sup> healthy young adults,<sup>60</sup> healthy older adults,<sup>7,60</sup> and individuals with Parkinson's disease<sup>61</sup> and Huntington disease.<sup>62</sup>

For younger adults, the GaitMat II was approximately 12 m in length. The initial and final 2 m were inactive sections to allow for acceleration and deceleration of the participant. The middle 8 m were active and used for data collection. For older adults, the GaitMat II was approximately 8 m in length. The initial and final 2 m were inactive sections to allow for acceleration and deceleration of the participant. The middle 4 m were active and used for data collection.

Each participant completed two practice walks the length of the walkway to become familiar to walking on mat. Each walk was considered one pass. Four passes were collected at the subject's self-selected walking speed for data collection. Participants completed two test sessions approximately one week apart.

### **3.2.3 Data processing**

GaitMat II data were inspected and cleaned for half foot-prints (footprints that occur at the beginning and the end of the mat) and extraneous points. Step length, step width, step time, stance time, swing time, and double support time were determined for each individual step. These spatial and temporal gait characteristics were commonly used in studies of gait variability.<sup>7,25,28,44,48</sup> We first looked for asymmetries between left and right steps, as asymmetries can impact measures of gait variability.<sup>120</sup> There were no asymmetries between left and right steps, so left and right steps were combined and the standard deviation from all steps was calculated as the measure of gait variability.



### 3.2.4 Statistical analysis

All statistical analyses were conducted with SAS<sup>®</sup> version 9.3 (SAS Institute, Inc., Cary, North Carolina). We computed appropriate descriptive statistics to describe the study sample. The mean and standard deviation of gait variability of spatial and temporal gait characteristics for younger and older adults were calculated. Absolute differences of gait variability between visit 1 and visit 2 were computed. Independent sample *t*-tests were used to compare the absolute differences between younger and older adults.

To assess test-retest reliability of gait variability in younger and older adults, intra-class correlation coefficients (ICCs) (2, 1 model) were computed. ICCs were interpreted as follows: less than 0.4, poor; 0.4 to 0.75, fair to good; and more than 0.75, excellent.<sup>165</sup> ICCs represent the relative reliability which is the degree to which individuals maintain their test results in a sample with repeated measurements.<sup>121</sup>

Given that ICCs may be affected by limited range of data,<sup>51</sup> especially among younger adults, absolute measures of reliability were also calculated. Absolute reliability, which reflects agreement (i.e. measurement error occurring with repeated testing), was assessed using the following analyses: 95% limits of agreement (95% LoA) in conjunction with Bland-Altman plots, relative limits of agreement (LoA%) and standard error of measurement (SEM).<sup>120,121</sup> 95% limits of agreement (95% LoA) express the degree of error proportional to the mean in the measurement units, and was calculated as follows: 95% LoA= Mean  $\pm$  2SD.<sup>52</sup> Bland-Altman plots were generated to provide a visual presentation of gait variability by plotting the difference of gait variability measured at visit 1 and visit 2 against the average of gait variability from visit 1 and visit 2.<sup>52</sup> Relative limits of agreement (LoA%) express the absolute difference of gait

variability measured at visit 1 vs visit 2 as a percentage of the group mean of gait variability measured at visit 1 and visit 2.<sup>56,120</sup> Standard error of measurement (SEM) quantifies the error in the units of the measured variable, and was computed as follows:  $SD_{\text{pooled}} \times \text{SQRT}(1-ICC)$ , where SD is the pooled standard deviation of test-retest measures, and the ICC is the calculated intra-class coefficient correlation for the test-retest measures.<sup>121</sup>

We also calculated the minimal detectable change (MDC) which is the smallest change that indicates a real change in an individual beyond that attributed to measurement error. The MDC at 90% and 95% level were calculated using the following equations:  $MDC_{90} = SEM \times 1.65 \times \text{SQRT}2$ ;  $MDC_{95} = SEM \times 1.96 \times \text{SQRT}2$ .<sup>162</sup>

### **3.3 RESULTS**

#### **3.3.1 Participants characteristics**

Younger adults (10 male and 30 female), with a (mean  $\pm$  standard deviation) age of  $26.6 \pm 6.0$  years were included in the study. Older adults (11 male and 35 female), with age  $78.1 \pm 6.2$  years were included in the study. On average, older adults walked slower, with a shorter step length and a wider step width compared to younger adults (Table 4).

#### **3.3.2 Gait variability of spatial and temporal gait characteristics**

The mean gait variability of spatial gait characteristics for younger and older adults ranged 0.02-0.03 m and for temporal gait characteristics ranged 0.02-0.04 s. Younger adults were less

variable and had a smaller range of values compared to older adults. The absolute differences of gait variability between visits 1 and 2 were greater in older adults compared to younger for all gait variables. The absolute differences of gait variability between visits 1 and 2 were significantly different between younger and older adults for all gait variables except step length and stance time (Table 5).

### **3.3.3 Reliability and minimal detectable change of spatial and temporal gait variability**

Intra-class correlation coefficients of gait variability (ICCs) ranged 0.26-0.65 in younger and 0.28-0.74 in older adults. In younger adults, step length was the most reliable with ICC = 0.65, whereas swing time was the least reliable with ICC = 0.26. In older adults, stance time was the most reliable with ICC = 0.74 and step length was the least reliable with ICC = 0.28 (Table 6).

Relative limits of agreement (LoA%) were consistently higher (i.e. less reliable) for all gait variables in older compared to younger adults. Relative limits of agreement (LoA%) ranged from 16.7% to 24% in younger adults and from 26.7% to 40% in older adults (Table 6). In younger adults, step length was the most reliable with LoA% = 16.7%, whereas step width was the least reliable with LoA% = 24%. In older adults, step width and double support time were the most reliable with LoA% = 26.7% and step time and swing time were the least reliable with LoA% = 40% (Table 6). The SEM were consistently higher (i.e. less reliable) for all gait variables in older adults compared to younger except for step width. The MDC was consistently larger for all gait variables in older adults compared to younger except for step width. Fig. 4 illustrates the Bland-Altman plot for step time variability and plots of other spatial and temporal

gait variability were similar. The Bland Altman plots showed that there was no negative or positive trend; however, participants with greater gait variability tended to be less reliable.

The gait variability values for younger adults were calculated using a mean of 38 steps, whereas for older adults the gait variability values were calculated using a mean of 23 steps. To ensure the number of steps used in the calculation of gait variability did not impact our results, we repeated the analysis using the same number of steps for younger and older adults (number of steps = 23). Sensitivity analyses including the same number of steps in the calculations for younger and older adults did not significantly alter the findings.

### **3.4 DISCUSSION**

When examining the test-retest reliability of spatial and temporal gait variability in younger and older adults using both absolute and relative reliability our findings were inconsistent. Using a relative measure of reliability, the ICCs, reliability of gait variability ranged from poor to fair in both younger and older adults, whereas using absolute measures of reliability, the younger were more reliable than the older adults. The discrepancy between relative and absolute measures of reliability highlights an important difference between the approaches. A low ICC may be obtained in situations where there is a small range of values in the sample and does not necessarily mean that a test is not acceptable<sup>60</sup> as ICC is influenced by the heterogeneity of the sample and variability of data.<sup>52,121</sup> Given the limited range in the younger adults in our sample, the ICC may not be the best measure of reliability. In contrast, absolute reliability statistics are not affected by these sample characteristics; therefore, the discussion will focus on the absolute

reliability findings. Similar studies who have examined the reliability of gait variability and dealt with issues of limited range data have also reported absolute reliability.<sup>56,120,125,166</sup>

Younger adults had smaller absolute differences compared to older adults in all gait variability parameters. Also, with LoA% and SEM younger adults were consistently more reliable than the older adults in all gait variables except SEM for step width. The MDC<sub>90</sub> and MDC<sub>95</sub> values were consistently lower in younger adults compared to the older adults in all gait variables except step width. These results of absolute reliability and MDC support our hypothesis that younger adults are more stable from time to time and fluctuate less over time compared to older adults. Therefore, our findings suggest that in older adults, some age-related decline in the organization and stability of the gait cycle is expected, which may be indicative of the overall health and control of the locomotor system. The findings also help to expand our knowledge about reliability and minimal detectable change of gait variability in younger and older adults. Furthermore, the current findings may suggest the use of spatial and temporal gait variability as a valuable measure for assessing the stability of the locomotor system.

To our best knowledge, no previous study has investigated the test-retest reliability and the MDC of gait variability in healthy young and older adults in the same analysis. Previous studies investigated the reliability and MDC of gait variability either only in young or only in older adults.<sup>8,56,120,166</sup> The majority of previous studies which investigated the test-retest reliability of gait variability report the ICC, which had limitations in our study sample.<sup>6,7,47,127</sup> Of the studies that investigated the test-retest reliability of spatial and temporal gait variability, only Galna et al. examined similar gait variability characteristics as our study and reported relative limits of agreement (LoA%) as a measure of absolute reliability.<sup>120</sup> When comparing LoA% of

gait variability for healthy older adults during intermittent walks, our values were lower than Galna et al. In our study (n= 46), LoA% ranged from 26.7% to 40%, whereas Galna et al<sup>120</sup> (n= 27) reported LoA% ranged from 55% to 87%, the higher (greater) values of LoA% which represent poorer absolute reliability may be partly explained by the smaller sample size.

Interestingly, the Bland Altman plots showed that in older adults greater gait variability was associated with a greater difference in gait variability from visit 1 to visit 2 (i.e. greater inconsistency). However, many of the older adults with low gait variability had a small difference in gait variability from session to session (i.e. consistent gait variability) which is similar to the younger participants.

### **3.4.1 Study limitations**

Potential limitations of this study should be acknowledged. First, gait variability was collected during intermittent walks with a limited number of passes. Testing protocol can impact the reliability of gait variability. Recently, Galna et al. suggested using a continuous walking protocol instead of short intermittent walks with no fewer than 30 steps to improve the reliability of gait variability.<sup>120</sup> The purpose of our study was to compare the reliability of gait variability between younger and older adults, as commonly measured over short distances, and not to maximize the reliability estimate of gait variability. Second, the SEM and the MDC results in our study should be interpreted with caution since the ICC is used in their calculations. In our study, the ICCs may have been influenced by a limited range of values.

Future research should further investigate inconsistency of gait variability as a potential early indicator of a decline in mobility. For example, measuring gait variability at more frequent

time intervals whether it's daily or hourly to see if this inconsistency in gait variability is a true phenomenon which could be a marker of early decline in the locomotor control and stability and not simply an indicator of a measurement error.

### **3.5 CONCLUSION**

Younger adults had greater test-retest reliability and smaller MDC of spatial and temporal gait variability compared to older thus supporting the hypothesis that younger are more stable and fluctuate less over time compared to older adults.

**Table 4. Characteristics of younger and older participants.**

<b>Characteristics</b>	<b>Younger (n=40)</b>	<b>Older (n=46)</b>	<b>P value</b>
<b>Demographics</b>			
Age (years)	26.60 (6.0)	78.09 (6.2)	0.000*
<b>Gait Characteristics</b>			
Gait speed (m/s)	1.29 (0.19)	0.95 (0.28)	0.000*
Step length (m)	0.70 (0.06)	0.53 (0.12)	0.000*
Step width (m)	0.04 (0.02)	0.06 (0.04)	0.008*
Step time (s)	0.55 (0.05)	0.58 (0.10)	0.082
Swing time (s)	0.42 (0.03)	0.44 (0.05)	0.009*
Stance time (s)	0.69 (0.07)	0.73 (0.15)	0.140
Double support time (s)	0.13 (0.03)	0.14 (0.06)	0.375

Note: Values are mean (standard deviation) unless otherwise noted.

\* A significant difference ( $p < 0.05$ ) between characteristics of younger and older adults using independent sample *t*-test



**Table 5. Description of variability of gait characteristics for younger and older adults, mean±standard deviation (range).**

<b>Gait variability</b>	<b>Younger</b>		<b>Older</b>		<b>Absolute difference between visit 1 and visit 2</b>		<b>P value</b>
	<b>Visit 1</b>	<b>Visit 2</b>	<b>Visit 1</b>	<b>Visit 2</b>	<b>Younger</b>	<b>Older</b>	
<b>Step length (m)</b>	0.03±0.01 (0.02-0.05)	0.03±0.01 (0.02-0.04)	0.03±0.02 (0.02-0.14)	0.03±0.01 (0.02-0.06)	0.005±0.003	0.009 ±0.016	0.081
<b>Step width (m)</b>	0.02±0.01 (0.01-0.04 )	0.03±0.01 (0.02-0.04)	0.03±0.01 (0.01-0.06)	0.03±0.01 (0.01-0.07)	0.006±0.004	0.008±0.009	0.021*
<b>Step time (s)</b>	0.03±0.01 (0.01-0.04)	0.03±0.01 (0.01-0.05)	0.03±0.02 (0.01-0.09)	0.03±0.02 (0.01-0.08)	0.006±0.004	0.012±0.014	0.002*
<b>Swing time (s)</b>	0.02±0.004 (0.02-0.04)	0.02±0.005 (0.02-0.03)	0.03±0.02 (0.01-0.11)	0.03±0.02 (0.01-0.09)	0.004±0.004	0.012±0.016	0.001*
<b>Stance time (s)</b>	0.03±0.01 (0.02-0.06)	0.03±0.01 (0.02-0.06)	0.04±0.02 (0.02-0.09)	0.04±0.02 (0.02-0.11)	0.007±0.006	0.011±0.009	0.071
<b>Double support time (s)</b>	0.02±0.003 (0.01-0.03)	0.02±0.004 (0.01-0.03)	0.03±0.01 (0.01-0.06)	0.03±0.02 (0.01-0.09)	0.004±0.002	0.008±0.009	<.0001*

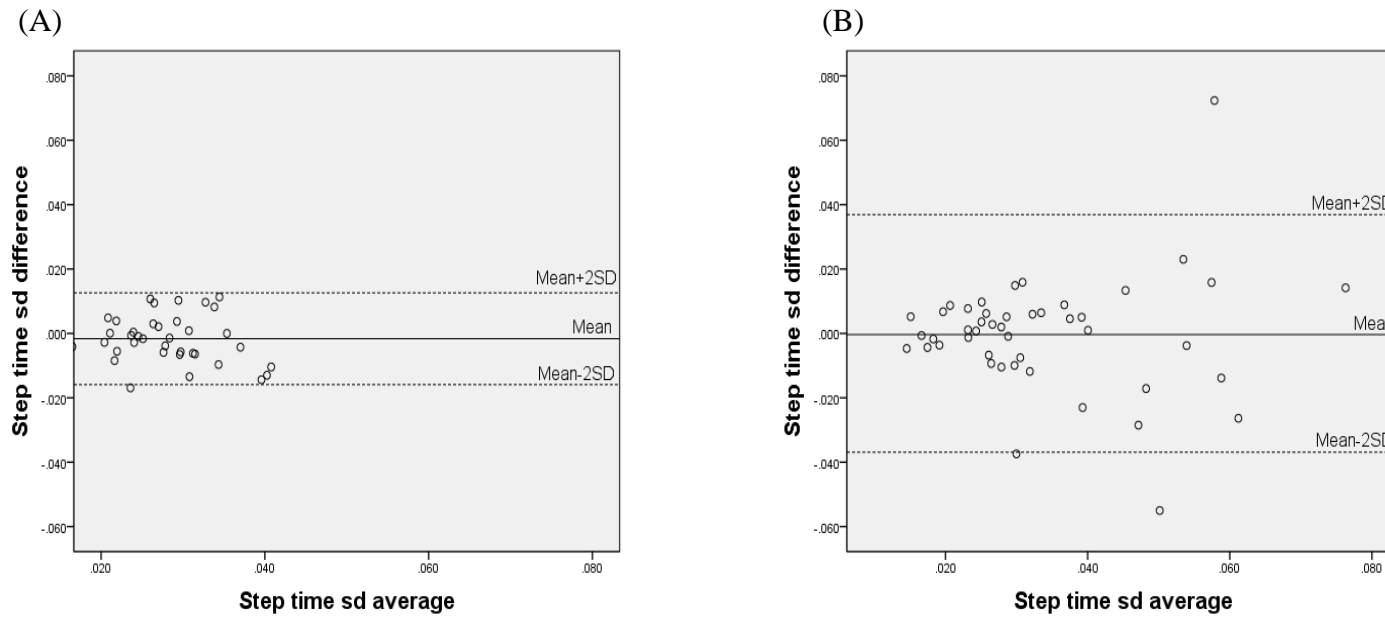
Absolute difference is the absolute difference of spatial and temporal gait variability between visit 1 and visit 2.

\* A significant difference ( $p < 0.05$ ) of the absolute differences between younger and older adults using independent sample *t*-tests.

**Table 6. Test-retest reliability and MDC of gait variability for younger and older adults.**

Gait variability	ICC (CI 95%)		95% LoA		LoA%		SEM		MDC <sub>90</sub>		MDC <sub>95</sub>	
	Younger	Older	Younger	Older	Younger	Older	Younger	Older	Younger	Older	Younger	Older
<b>Step length (m)</b>	0.65 (0.43, 0.80)	0.28 (0.00, 0.52)	-0.012 to 0.011	-0.036 to 0.039	16.7	30.0	0.006	0.017	0.014	0.040	0.016	0.047
<b>Step width (m)</b>	0.29 (0.03, 0.56)	0.50 (0.24, 0.68)	-0.016 to 0.011	-0.025 to 0.023	24.0	26.7	0.008	0.007	0.020	0.017	0.023	0.020
<b>Step time (s)</b>	0.54 (0.29, 0.73)	0.43 (0.15, 0.64)	-0.016 to 0.013	-0.037 to 0.036	20.0	40.0	0.007	0.015	0.016	0.035	0.019	0.042
<b>Swing time (s)</b>	0.26 (0.00, 0.53)	0.36 (0.07, 0.58)	-0.012 to 0.010	-0.040 to 0.040	20.0	40.0	0.004	0.016	0.009	0.037	0.000	0.044
<b>Stance time (s)</b>	0.56 (0.30, 0.74)	0.74 (0.57, 0.84)	-0.020 to 0.016	-0.025 to 0.030	23.3	27.5	0.007	0.010	0.015	0.024	0.018	0.028
<b>Double support time (s)</b>	0.45 (0.17, 0.66)	0.38 (0.10, 0.60)	-0.009 to 0.007	-0.036 to 0.033	20.0	26.7	0.003	0.008	0.006	0.018	0.007	0.022

Abbreviations: ICC, Intra-class correlation coefficient; CI 95%, 95% confidence interval for the ICC; 95% LoA, Bland and Altman 95% limits of agreement; LoA%, relative limits of agreement; SEM, standard error of measurement; MDC<sub>90</sub>, minimal detectable change with a confidence level of 90%; MDC<sub>95</sub>, minimal detectable change with a confidence level of 95%.



**Figure 4. Bland-Altman plots of step time variability difference vs average step time variability with 95% limits of agreements in (A) younger and (B) older adults.**

#### **4.0 CHALLENGING THE MOTOR CONTROL OF GAIT: GAIT VARIABILITY DURING SLOWER AND FASTER PACE WALKING CONDITIONS IN YOUNGER AND OLDER ADULTS**

**Background.** Gait variability is a measure of motor control of gait. Little is known about age-related changes in the motor control of gait (gait variability) during challenging walking conditions, such as slower and faster pace walking.

**Objective.** The purpose of this study was to examine the impact of challenging walking conditions (slower and faster speeds) on gait variability in younger and older adults.

**Study design.** This study was a cross-sectional, observational design.

**Methods.** Forty younger (mean age =  $26.6 \pm 6.0$  years) and 111 community-dwelling older adults (mean age =  $77.3 \pm 6.0$  years), independent in ambulation, were studied. Gait characteristics were collected using a computerized walkway (GaitMat II™). Step length, step width, step time, swing time, stance time and double support time variability were derived as the standard deviation of all steps across the 4 passes.

**Results.** Compared to younger, older adults had a significant change in their gait variability from usual to slower in step width ( $-0.006 \pm 0.003$ ), step time ( $0.028 \pm 0.006$ ), swing time ( $0.023 \pm 0.004$ ), stance time ( $0.042 \pm 0.008$ ), and double support time ( $0.024 \pm 0.005$ ). Changes in gait variability from usual to faster were not significantly different between younger and older adults.

**Conclusions.** Walking slowly is more challenging to the motor control of gait and may be more sensitive to age-related declines in gait than usual and faster speed walks.

**Keywords.** Gait variability; Motor control; Older adults; Faster; Slower

## 4.1 INTRODUCTION

Gait variability, defined as fluctuations in spatio-temporal gait characteristics from one step to the next, is a measure of the motor control of gait.<sup>21</sup> Under normal conditions within a testing session, the values of these fluctuations are relatively small reflecting remarkable consistency and stability within the locomotor system.<sup>1</sup> However, the fluctuations in spatio-temporal gait characteristics are altered in normal aging,<sup>23-25</sup> in certain disorders that are largely considered having difficulties in the motor control of gait (i.e. Parkinson's and Alzheimer disease)<sup>26,27</sup> as well as in subclinical conditions.<sup>21,29</sup> Assessment of the alterations in gait variability may provide additional insights about mobility dysfunction and fall risk, above and beyond mean values of gait parameters such as average gait speed or step time.<sup>1,6,30,31</sup>

Measures of gait variability are commonly used to study age-related gait changes.<sup>23,28,30,48,145</sup> Although some studies have found gait variability to be greater in older adults compared to younger adults,<sup>44,118</sup> others have reported no differences in gait variability between younger and older adults.<sup>21,48,111,167</sup> The majority of the studies that did not find a difference in gait variability between younger and older adults,<sup>21,48,111</sup> investigated gait variability during usual pace unchallenged walking where energy cost of walking is minimized.<sup>141</sup> This optimization of walking at usual speed might be due to the inherent

interaction of neural and biomechanical mechanisms, with only minimal active control of high-level sensory feedback control.<sup>142</sup>

Little is known about age-related changes in gait variability during challenging walking conditions such as slower and faster pace walking. It is likely that these challenging walks place a greater demand on motor control of gait and hence may be more sensitive to age-related declines in gait compared to usual walking speed.<sup>9,10</sup> Healthy younger adults become more variable when they walk at slower speed.<sup>139,143</sup> Slowing of walking speed is one of the most consistent reported age-related changes in gait.<sup>98</sup> Therefore, increased gait variability in healthy older adults may be simply related to their slow walking speed. Alternatively, several studies suggest that the alterations in gait variability with older adults are a reflection of underlying subclinical pathology in important neural locomotor regions, and not simply a manifestation of slow walking speed.<sup>1,32,84</sup> Slower speed of walking might be a challenging task to their motor control of gait. In addition, faster walking speed has been previously reported in the guidelines for clinical spatio-temporal gait analysis in older adults as a highly stressful walking condition that may challenge older adults and optimize the detection of high-level gait impairment.<sup>9,168</sup>

Previous studies which examined gait variability at different walking speeds in younger and older adults obtained conflicting results, as some failed to find any relationship,<sup>92,116</sup> while others reported either linear or a non-linear relationship.<sup>114,144</sup> Additionally most of these studies examined gait variability with fixed walking speeds on a treadmill. The imposed constant speed of a treadmill may artificially impose motor control of gait and impede the natural variation that occurs during over-ground walking and therefore minimize gait variability.<sup>44,132</sup>

The association between over-ground challenging walking conditions (slower and faster speeds) and gait variability remains unclear. Therefore, the purpose of this study was to examine the impact of challenging over-ground walking conditions (slower and faster speeds) on gait variability in younger and older adults. We expected gait variability would be greater under challenging walking conditions of slower and faster speeds compared to usual speed, and the impact would be greater in older adults compared to younger adults. To explore the impact of age-related changes on gait variability independent of walking speeds, we also compared gait variability by challenging walking condition for a subgroup of older adults who had similar walking speeds as the younger adults (i.e. speed-matched older adults). The assessment of gait variability during challenging walking conditions such as walking slower or faster may uncover motor control deficits among older adults that are not identified during usual walking testing.

## **4.2 METHODS**

### **4.2.1 Participants**

Forty younger and 111 older adults participated in the study. The younger adults were recruited through fliers posted throughout the University of Pittsburgh. The younger participants were between the ages of 18 and 50, ambulated independently, and had no diagnosed neuromuscular, cardiopulmonary, or orthopedic conditions that would affect walking. The younger participants were first screened over the phone to determine initial eligibility. Subjects who passed the phone screen were scheduled for a one hour clinic visit which included a physical exam (range of

motion and muscle testing) to determine final eligibility followed by measurement of gait characteristics using a computerized walkway.

Older participants were identified from a previous prospective longitudinal study of gait and balance in older adults.<sup>164</sup> The inclusion criteria for the older adults were age 65 or older; self-reported ability to tolerate a five-hour session (with rest periods) of answering questionnaires and performing walking tests; ability to independently walk a household distances (approximately 50 ft) at a minimum, with or without an assistive device and without the assistance of another person. Also, the older adults had to be free of (a) neuromuscular disorders that impaired movement (including but not limited to Parkinson's disease, stroke, and multiple sclerosis); (b) cancer with active treatment (specifically radiation or chemotherapy) within the past 6 months; (c) non-elective hospitalization for a life-threatening illness or major surgical procedure in the past 6 months; (d) severe pulmonary disease requiring supplemental oxygen or resulting in difficulty breathing at rest or with minimal exertion (such as walking between rooms in their home); and (e) chest pain with activity or a cardiac event, such as heart attack within the past 6 months. The older participants were first screened over the phone to determine initial eligibility. Subjects who passed the phone screen were scheduled for a clinic visit which included a physical exam to determine final eligibility. Older adults completed 5 h of testing, including a measurement of gait characteristics which occurred within the first hour of testing. Both studies of younger and older adults were approved by the University of Pittsburgh Institutional Review Board, and all participants provided informed consent prior to participation.



#### 4.2.2 Gait characteristics

Spatial and temporal gait characteristics were collected using a computerized walkway (GaitMat II™) (EQ Inc, Chalfont, PA).<sup>37</sup> The GaitMat II is an automated gait analysis system, based on the opening and closing of pressure sensitive switches on the walkway that are displayed on the computer screen as footprints when the participant walks. The GaitMat II provides a temporal resolution of 5 ms and a spatial resolution of 15 mm in both the longitudinal and transverse directions. The reliability and validity of the computerized walkway has been established for quantification of the spatial and temporal mean gait characteristics for a variety of populations including children,<sup>59</sup> healthy young adults,<sup>60</sup> healthy older adults,<sup>7,60</sup> individuals with Parkinson's disease<sup>61</sup> and Huntington disease.<sup>62</sup>

For younger adults, the GaitMat II was approximately 12 m in length. The initial and final 2 m were inactive sections to allow for acceleration and deceleration of the participant. The middle 8 m were active and used for data collection. For older adults, the GaitMat II was approximately 8 m in length. The initial and final 2 m were inactive sections to allow for acceleration and deceleration of the participant. The middle 4 m were active and used for data collection.

*Testing conditions.*—Gait variability data were collected at various walking speed conditions expected to affect gait variability. Each participant completed two practice walks the length of the walkway for each walking speed condition to become familiar to walking on mat. Each walk was considered one pass. After practice trials, four passes were collected at each walking speed condition. Each participant completed the following walking speed conditions: *Slower self-*

*selected walking speed:* participants were instructed to walk as slow as they could without stopping.

*Usual self-selected walking speed:* participants were instructed to walk at a pace that represented their usual walking speed (as if they completed various tasks throughout their daily routines).

*Faster self-selected walking speed:* participants were asked to walk as fast as they could without running or putting themselves at risk of falling.

### **4.2.3 Data processing**

GaitMat II data were inspected and cleaned for half foot-prints (footprints that occur at the beginning and the end of the mat) and extraneous points. Step length, step width, step time, stance time, swing time, and double support time were determined for each individual step. These spatial and temporal gait characteristics were commonly used in studies of gait variability.<sup>7,25,28,44,48</sup> We tested for asymmetries between left and right steps using paired *t*-test, as asymmetries can impact measures of gait variability.<sup>120</sup> No asymmetries between left and right steps were found. Therefore, left and right steps were combined and the standard deviation from all steps was calculated as the measure of gait variability.

### **4.2.4 Statistical analysis**

All statistical analyses were conducted with SAS<sup>®</sup> version 9.3 (SAS Institute, Inc., Cary, North Carolina). We computed appropriate descriptive statistics to describe the study sample. We first fit a mixed linear model using the SAS<sup>®</sup> MIXED procedure with each measure of gait variability as the response variable; age group, walking speed condition, and age group  $\times$  walking speed

condition interaction as fixed effects of interest; and a participant random effect to account for the same participants performing under multiple conditions and the resulting stochastic nonindependence of observations. Appropriate contrasts were constructed to compare age groups within each walking speed condition; compare walking speed condition within each age group; and compare age groups in terms of usual to slower/faster differences (ie. components of the interaction term). To ensure the soundness of our statistical approach, we examined the residuals from the mixed models and constructed normal probability plots to determine if they were normally distributed. Next, we added usual walking speed as an additional continuous fixed effect covariate to the models to examine whether age group and walking speed condition differences in gait variability remained significant independent of usual walking speed.

In an attempt to further control for walking speed, we identified a subgroup of older adults who had similar walking speeds at usual and slower pace as the younger participants. Gait speed cut points of  $\geq 1.10$  m/s for usual speed and  $\geq 0.73$  m/s for slow speed were used to create the group of speed-matched older adults ( $n = 28$ ). These cut points were determined as the mean gait speed at usual for younger adults minus one SD and the mean gait speed at slower for younger adults minus one SD. We were unable to also match on faster walking speed in that very few older adults had similar faster speed as the younger ( $n < 10$ ). We then repeated the same analyses comparing the speed-matched older adults to the younger adults.

To help understand our findings regarding step width variability, we conducted a post hoc analysis to examine the impact of changing walking speeds (i.e. slower or faster) on mean step width in younger and older adults.

## **4.3 RESULTS**

### **4.3.1 Participant Characteristics**

Participant characteristics are shown in Table 7. At all three walking speed conditions the younger participants walked faster compared to older adults. The speed-matched older adults had similar slower and usual mean gait speeds as the younger adults (0.91 m/s and 1.28 m/s respectively). Younger, older, and speed-matched older adults were able to change their speeds appropriately for the different walking speed conditions. On average the difference between usual and slower was 0.39 (0.11) m/s for younger, 0.45 (0.25) m/s for older adults and 0.39 (0.16) m/s for speed-matched older adults. The mean difference between faster and usual was 0.47 (0.14) m/s for younger, 0.25 (0.15) m/s for older adults and 0.23 (0.14) m/s for speed-matched older adults.

### **4.3.2 Gait variability between younger and older adults at slower, usual and faster walking speed**

At usual walking speed, older adults were more variable than younger adults only in step length and step width whereas at slower walking speed, older adults were significantly more variable than younger adults in all gait characteristics. At faster walking speed, older adults were more variable than younger adults only in step width. When the analyses were adjusted for usual walking speed, the results were similar (Table 8).

The gait variability values for younger adults were calculated using a mean of 38 steps, whereas for older adults the gait variability values were calculated using a mean of 23 steps. To

ensure the number of steps used in the calculation of gait variability didn't impact our results, we repeated the analysis using the same number of steps for young and older adults (number of steps= 23). Sensitivity analyses including the same number of steps in the calculations for younger and older adults did not significantly alter the findings.

#### **4.3.3 Gait variability across slower, usual and faster walking speeds for younger and older adults**

Younger adults were more variable at slower speed compared to usual speed in step time and stance time. Younger adults were more variable at faster speed compared to usual speed only in step length. Older adults were more variable at slower speed compared to usual speed in all gait characteristics except for step width; in which they were less variable. There was no difference of gait variability in any of the gait characteristic between faster and usual speed in older adults (Table 9).

#### **4.3.4 Change in gait variability from usual to slower and usual to faster, between younger and older adults**

Older adults had a change in their gait variability in all gait characteristics except step length when they walked at slower walking speed compared to younger. Older adults did not have a change in their gait variability when they walked at faster speed compared to younger (Table 10).

#### **4.3.5 Gait variability between younger and speed-matched older adults at slower, usual and faster walking speed**

At usual walking speed, speed-matched older adults were more variable than younger adults for only step length and step width. At slower walking speed, compared to younger adults, speed-matched older adults were more variable in all gait characteristics except step time and stance time and at faster walking speed, speed-matched older adults were significantly more variable only for step width compared to the younger adults (Table 11).

When examining the change in gait variability from usual to slower walking speed, speed matched older adults had a greater increase only in swing time variability compared to the younger adults. When examining the change from usual to faster walking speeds, speed matched older adults had a greater increase in step width variability compared to the younger adults (Table 12).

#### **4.3.6 Impact of walking speed on mean step width**

In an attempt to explain why step width variability decreased with challenging walking conditions in older adults (which was opposite direction to the other gait characteristics), we examined the impact of various walking speed conditions on mean step width. For younger adults, mean step width was similar across all walking speed conditions (mean step width at slower = 0.041 m, at usual = 0.039 m, and at faster = 0.037 m). For older adults, step width mean was widest during slower walking speed compared to usual and faster speeds (mean step width at slower = 0.062 m, at usual = 0.048 m, and at faster = 0.046 m).

## 4.4 DISCUSSION

### 4.4.1 Gait variability at usual and at challenging walking conditions between younger and older adults

Age-related changes in spatial and temporal gait variability provide important information on the health of the locomotor system that control normal walking.<sup>1</sup> However, some studies have found no differences in gait variability between healthy younger and older adults during usual walking speed.<sup>21,48,111</sup> In one of the earliest studies investigating the effect of age on gait variability, Gabell and Nayak (1984) reported that gait variability for step length, stride width, stride time and double support time were not significantly different between younger and older adults. Similarly, Hausdroff et al. reported no differences in the gait variability between younger and older adults in stride time, stance time and swing time gait characteristics during a usual over-ground walking.<sup>48</sup> Consistent with those results, we found no differences in gait variability between younger and older adults for all gait characteristics during usual speed except for step length and step width (spatial gait characteristics). The small difference in gait variability we found between younger and older adults in our study implies that usual walking speed might not alter the motor control of gait responsible for fine tuning the spatial and temporal aspects of gait on a step to step basis in healthy aging.

The need for challenging walking conditions to distinguish between healthy younger and older adults has been recently highlighted.<sup>9,24,167,169</sup> We set out to examine the impact of challenging walking conditions on gait variability in younger and older adults. Our finding showed that older adults were more variable when they walked at slower speed compared to younger adults in all spatial and temporal gait characteristics (all  $p < 0.05$ ). Significant changes

in gait variability from usual to slower were presented in older adults compared to younger for all gait characteristics except for step length. However, at faster speed, older adults were more variable compared to younger adults only in step width. In contrast to what we hypothesized, changes in gait variability from usual to faster were not different between younger and older adults. Older adults increased their speed only by 0.25 m/s which may be not enough challenge to the motor control of gait to bring up changes in gait variability whereas younger adults increase their speed by 0.47 m/s. There could be a number of reasons why older adults did not speed up as much as the younger adults one of which may be fear as we instructed the participants to walk as fast as they could without putting themselves at risk of falling.

#### **4.4.2 Spatial and temporal gait variability during challenging walking conditions**

To better evaluate the present results and the potential clinical utility of gait variability, it will be helpful to understand what gives rise to the change in gait variability in all temporal gait characteristics from usual to slow pace walking (ie. greater impact) in older adults. Martin and colleagues found associations between poorer executive function/attention and processing speed with temporal, but not spatial, gait variability measures.<sup>42</sup> This is consistent with previous findings of increasing stride time variability, but not stride length variability, under dual-task cognitive interference.<sup>75</sup> Thus suggesting that stronger associations between executive function/attention and temporal versus spatial variability measures may be due to the timing component of the cognitive tests.<sup>86</sup> Given the significant change in gait variability in all temporal gait characteristics from usual to slower pace walking in older adults, one might speculate that examining gait variability at slower speed may be a more sensitive test for capturing and



predicting decline in cognitive function than examining gait variability at usual walking speed.

Younger adults were significantly more variable in step time and stance time during the slower speed compared to the usual speed. Previous studies have reported that slower walking is an attention-demanding task even in healthy young adults due to reduced gait automaticity and higher cortical control with changes in muscle activity pattern.<sup>10,170</sup> This may suggest that the healthy younger adults devote a part of their attention resources to the control of the stepping mechanism at self-selected slower speed.<sup>10</sup> However, underlying mechanisms of spatial and temporal gait variability during slower and faster walking speeds are still unclear.

#### **4.4.3 Gait variability between younger and speed-matched older adults**

In several studies the investigators argued that the greater gait variability demonstrated by older adults compared to younger is due to the possible confounding effect of slow walking speed,<sup>117,145,147</sup> because older adults typically walk slower.<sup>98</sup> In the current study, the older adults in general walked slower than the younger (i.e., usual gait speed = 1.07 m/s for older vs. 1.29 m/s for younger). To determine if the differences in gait variability between younger and older were attributed to the differences in usual gait speed, we adjusted for usual gait speed in the analyses. The differences in gait variability between younger and older remained after adjusting for differences in usual gait speed. In addition to statistically adjusting for usual gait speed, we further controlled for walking speed by selecting a subgroup of older adults (speed-matched older adults) who had similar gait speeds to the younger adults at usual and slow (i.e., usual gait speed = 1.28 m/s and slow gait speed = 0.91 m/s). Even though gait speeds were similar at usual and slower, the speed-matched older adults were more variable in all gait characteristics except

step time and stance time at slower speed compared to the younger adults. At slower speed, the differences in the gait variability between younger and speed-matched older adults remained significant for step length, step width, swing time and double support time, thus indicating that the differences in gait variability at the slower speed are independent of the differences in walking speed. The increased gait variability demonstrated by older adults at slower walking speed may be related to underlying subclinical pathology in important neural locomotor regions, and not simply a manifestation of slower walking speed. Slower walking speed is a challenging task and may facilitate the detection of high-level gait impairment in older adults. Our findings about gait variability are similar to the work of Brach and colleagues who found that older adults who walked at a similar gait speed as the younger adults, were less smooth (i.e., poor motor control of gait) during challenging walking conditions (i.e., circle path and dual task). Their results indicate that the differences in smoothness of walking between the younger and older adults were independent of the differences in walking speed.<sup>3</sup> Furthermore, though not all statistically significant, the pattern of findings were similar for younger vs. speed-matched older adults when examining the change in gait variability from usual to slower. A significant change in gait variability from usual to slower pace walking was present only for swing time variability in speed-matched older adults compared to younger. A previous study had suggested that swing time variability may be used as a speed-independent marker of gait steadiness and fall risk in older adults.<sup>171</sup>

#### 4.4.4 Step width variability

Step width variability was consistently greater in older adults and speed-matched older adults compared to younger adults in all walking speed conditions. Gabell and Nayak suggest that step width variability is related to balance control mechanism and higher step width variability is indicative of impaired balance.<sup>21,30</sup> The greater step width variability for older adults compared to younger during the challenging walking conditions may indicate a challenge to the balance control system. However, our finding contradicts the findings of Kang & Dingwell, who didn't find a significant age-effect ( $p < 0.16$ ) for step width variability.<sup>92</sup> The discrepant finding may be due to the older participants in their study being relatively healthy with better mobility (ie, mean usual gait speed = 1.29 (0.15) m/s) than our participants. The slower mean gait speed and the greater standard deviation (mean usual gait speed = 1.07 (0.26) m/s) in our total sample of older adults ( $n = 111$ ) indicate that the participants in the current study were more limited than those studied by Kang & Dingwell.<sup>92</sup> Even though our speed-matched older adults had a similar usual gait speed (i.e. mean usual gait speed = 1.28 (0.15) m/s) to the participants in Kang & Dingwell study, they were more variable on step width during challenging walking conditions.<sup>92</sup> It is possible that the conflicting findings may be due, in part, to testing methodology, in that in the Kang & Dingwell study walking was tested on a treadmill whereas in the current study walking was tested over-ground.<sup>92</sup>

On the other hand, older adults were less variable in step width during the slower speed compared to the usual speed. In addition to decreasing their step width variability, older adults increased their mean step width significantly during the slower speed compared to the usual speed (mean step width at slower speed = 0.062 m vs. mean step width at usual speed = 0.048

m). In younger adults, when they walked slower their mean step width didn't significantly change compared to usual speed (mean step width at slower speed = 0.039 m vs. mean step width at usual speed = 0.041 m). Most likely, the older adults were widening their step width as a strategy to persevere balance during the challenging walking condition (slower speed).

#### **4.4.5 Study limitations**

Some potential limitations of this study should be acknowledged. First, participants did not walk at a set speed. Gait variability was examined during self-selected over-ground walking, where subjects were directed to walk “slower”, “usual” and “faster”. The most common approach to control for walking speed is through treadmill walking. However, on the treadmill gait speed is constant, and perhaps this reduces the degrees of freedom and helps to minimize step-to-step variations compared to the over-ground walking.<sup>44,171</sup> Also, the treadmill acts as an external cue, which may decrease gait variability. For example, Dingwell et al. reported that stride time variability was significantly reduced in treadmill compared to over-ground walking in older adults.<sup>132</sup> Second, the differences in the number of steps between younger and older adults could be a potential limitation. However, sensitivity analyses including the same number of steps in the calculations between groups did not significantly alter the findings despite this measurement limitation. Another limitation is that the speed-matched older adults (n = 28) were part of a group from a previous study and therefore the sample could not be matched exactly to the younger subjects. Finally, the results of our study applied only for community dwelling older adults, and it is difficult to extrapolate the discussion for clinical populations.

Future longitudinal studies are needed to determine if changes in gait variability on challenging gait conditions predicts future mobility disability in older adults with near normal gait. Also, future studies are needed to investigate the impact of challenging walking conditions on different types of spatial and temporal gait variability independently because if underlying mechanisms of variable gait are better understood, then distinct interventions can be designed to address specific deficiencies. It is possible that individually designed therapeutic exercise programs based on the type of gait variability could result in greater improvements in walking function and overall mobility.<sup>40</sup>

## **4.5 CONCLUSION**

Walking slowly is challenging to the motor control of gait even in older adults with normal gait speed (i.e. speed-matched older adults). The challenge of walking slowly may identify early changes in the motor control of gait that are not obvious when examining gait during usual, preferred speed. When examining the motor control of gait, clinicians should consider examining gait under various walking speeds. These challenging walking tasks are often designed to target the consequences of aging on gait function. It appears the changes in gait variability (ie. impairment of the motor control of gait) in older adults are independent of slow walking speed. Many gait interventions focus on increasing gait speed alone. Clinicians may want to consider interventions that not only focus on gait speed but also on the motor control of gait.

**Table 7. Characteristics of younger and older participants**

<b>Characteristics</b>	<b>Younger (n=40)</b>	<b>Older (n=111)</b>	<b>Speed-matched Older* (n=28)</b>
<b>Age (years)</b>	26.60 (6.0)	77.25 (6.0) <sup>†</sup>	75.2 (5.1) <sup>††</sup>
<b>Height (cm)</b>	168.4 (8.3)	163.4 (9.5)	165.2 (9.9)
<b>Weight (kg)</b>	66.4 (12.4)	77.4 (15.7)	76.4 (14.3)
<b>Female n (%)</b>	30 (75)	82 (73.9)	19 (67.9)
<b>White n (%)</b>	24 (60)	96 (86.5)	26 (92.9)
<b>Gait speed (m/s)</b>			
<i>Slower</i>	0.90 (0.17)	0.62 (0.24) <sup>†</sup>	0.91 (0.14)
<i>Usual</i>	1.29 (0.19)	1.07 (0.26) <sup>†</sup>	1.28 (0.15)
<i>Faster</i>	1.76 (0.22)	1.32 (0.34) <sup>†</sup>	1.52 (0.18) <sup>††</sup>

Note: Values are mean (standard deviation) unless otherwise noted.

\* Speed-matched old is a subgroup of older adults who had a usual gait speed  $\geq 1.10$  m/s and slower gait speed  $\geq 0.73$  m/s.

<sup>†</sup> A significant difference ( $p < 0.05$ ) between younger and old groups using independent sample *t*-tests.

<sup>††</sup> A significant difference between younger and speed matched older groups using independent sample *t*-tests.

**Table 8. Gait variability between younger and older adults at slower, usual and faster walking speed.**

<b>Gait Variability</b>	<b>Younger</b>	<b>Older</b>	<b>Unadjusted Difference (SE)</b>	<b>p Value</b>	<b>Adjusted Difference* (SE)</b>	<b>p Value</b>
<b>Step length (m)</b>						
<i>Slower</i>	0.027 (0.008)	0.038 (0.011)	0.011 (0.002)	<.0001	0.010 (0.002)	<0.0001
<i>Usual</i>	0.025 (0.007)	0.033 (0.014)	0.008 (0.002)	<.0001	0.007 (0.002)	0.001
<i>Faster</i>	0.030 (0.007)	0.034 (0.009)	0.004 (0.002)	.05	0.003 (0.002)	0.19
<b>Step width (m)</b>						
<i>Slower</i>	0.022 (0.006)	0.030 (0.013)	0.013 (0.003)	.003	0.010 (0.003)	<0.0001
<i>Usual</i>	0.024 (0.006)	0.037 (0.018)	0.008 (0.003)	<.0001	0.016 (0.003)	<0.0001
<i>Faster</i>	0.026 (0.006)	0.039 (0.016)	0.013 (0.003)	<.0001	0.016 (0.003)	<0.0001
<b>Step time (s)</b>						
<i>Slower</i>	0.038 (0.012)	0.070 (0.044)	0.032 (0.004)	<.0001	0.025 (0.004)	<.0001
<i>Usual</i>	0.027 (0.007)	0.030 (0.015)	0.004 (0.004)	.43	-0.003 (0.004)	0.46
<i>Faster</i>	0.026 (0.007)	0.029 (0.015)	-0.001 (0.004)	.88	-0.007 (0.004)	0.09
<b>Swing time (s)</b>						
<i>Slower</i>	0.030 (0.008)	0.058 (0.029)	0.028 (0.004)	<.0001	0.024 (0.004)	<.0001
<i>Usual</i>	0.024 (0.004)	0.028 (0.015)	0.005 (0.004)	.18	0.001 (0.004)	0.77
<i>Faster</i>	0.023 (0.004)	0.026 (0.020)	0.003 (0.004)	.44	-0.001 (0.004)	0.79
<b>Stance time (s)</b>						
<i>Slower</i>	0.050 (0.016)	0.097 (0.064)	0.047 (0.006)	<.0001	-0.007 (0.006)	<0.0001
<i>Usual</i>	0.032 (0.008)	0.037 (0.017)	0.005 (0.006)	.47	0.038 (0.006)	0.46
<i>Faster</i>	0.031 (0.009)	0.033 (0.021)	0.002 (0.006)	.72	-0.005 (0.006)	0.27
<b>Double support time (s)</b>						
<i>Slower</i>	0.028 (0.009)	0.057 (0.040)	0.029 (0.004)	<.0001	0.024 (0.004)	<.0001
<i>Usual</i>	0.020 (0.003)	0.024 (0.012)	0.005 (0.004)	.27	0.000 (0.004)	0.96
<i>Faster</i>	0.017 (0.003)	0.022 (0.018)	0.005 (0.004)	.25	0.000 (0.004)	1.0

\*Adjusted for usual over-ground walking speed.

**Table 9. Gait variability across slower, usual and faster walking speeds for younger and older adults.**

Gait variability	Slower	Usual	Faster	Slower vs. usual Difference (SE)	<i>p</i> Value	Faster vs. usual Difference (SE)	<i>p</i> Value
<b>Step length (m)</b>							
<i>Younger</i>	0.027 (0.008)	0.025 (0.007)	0.030 (0.007)	0.002 (0.002)	0.30	0.005 (0.002)	0.01
<i>Older</i>	0.038 (0.011)	0.033 (0.014)	0.034 (0.009)	0.005 (0.001)	<.0001	0.001 (0.001)	0.44
<b>Step width (m)</b>							
<i>Younger</i>	0.022 (0.006)	0.024 (0.006)	0.030 (0.007)	-0.002 (0.002)	0.45	0.002 (0.002)	0.37
<i>Older</i>	0.030 (0.013)	0.037 (0.018)	0.034 (0.009)	-0.007 (0.001)	<.0001	0.002 (0.001)	0.23
<b>Step time (s)</b>							
<i>Younger</i>	0.038 (0.012)	0.027 (0.007)	0.026 (0.007)	0.011 (0.005)	0.02	-0.001 (0.005)	0.87
<i>Older</i>	0.070 (0.044)	0.030 (0.015)	0.029 (0.015)	0.040 (0.003)	<.0001	-0.005 (0.003)	0.09
<b>Swing time (s)</b>							
<i>Younger</i>	0.030 (0.008)	0.024 (0.004)	0.023 (0.004)	0.006 (0.004)	0.08	-0.001 (0.004)	0.87
<i>Older</i>	0.058 (0.029)	0.028 (0.015)	0.026 (0.020)	0.030 (0.002)	<.0001	-0.003 (0.002)	0.23
<b>Stance time (s)</b>							
<i>Younger</i>	0.050 (0.016)	0.032 (0.008)	0.031 (0.009)	0.017 (0.007)	0.01	-0.001 (0.007)	0.88
<i>Older</i>	0.097 (0.064)	0.037 (0.017)	0.033 (0.021)	0.060 (0.004)	<.0001	-0.003 (0.004)	0.41
<b>Double support time (s)</b>							
<i>Younger</i>	0.028 (0.009)	0.020 (0.003)	0.017 (0.003)	0.008 (0.004)	0.05	-0.002 (0.004)	0.59
<i>Older</i>	0.057 (0.040)	0.024 (0.012)	0.022 (0.018)	0.032 (0.002)	<.0001	-0.002 (0.002)	0.41



**Table 10. Change in gait variability from usual to slower and usual to faster, between younger and older adults.**

<b>Gait Variability</b>	<b>Younger vs. older difference in usual to slower change</b>		<b>Younger vs. older difference in usual to faster change</b>	
	Difference (SE)	<i>p</i> Value	Difference (SE)	<i>p</i> Value
<b>Step length (m)</b>	0.003 (0.002)	0.18	-0.004 (0.002)	0.09
<b>Step width (m)</b>	0.006 (0.003)	0.04	0.000 (0.003)	0.88
<b>Step time (s)</b>	0.028 (0.006)	<.0001	-0.004 (0.006)	0.46
<b>Swing time (s)</b>	0.023 (0.004)	<.0001	-0.002 (0.004)	0.63
<b>Stance time (s)</b>	0.042 (0.008)	<.0001	-0.002 (0.008)	0.77
<b>Double support time (s)</b>	0.024 (0.005)	<.0001	0.000 (0.005)	0.97

**Table 11. Gait variability between younger and speed-matched older adults at slower, usual and faster walking speed.**

<b>Gait Variability</b>	<b>Younger</b>	<b>Speed-matched Older</b>	<b>Difference (SE)</b>	<b><i>p</i> Value</b>
<b>Step length (m)</b>				
<i>Slower</i>	0.027 (0.008)	0.033 (0.011)	0.006 (0.002)	0.00
<i>Usual</i>	0.025 (0.007)	0.031 (0.009)	0.005 (0.002)	0.01
<i>Faster</i>	0.030 (0.007)	0.032 (0.009)	0.001 (0.002)	0.49
<b>Step width (m)</b>				
<i>Slower</i>	0.022 (0.006)	0.038 (0.014)	0.016 (0.002)	<.0001
<i>Usual</i>	0.024 (0.006)	0.044 (0.014)	0.020 (0.002)	<.0001
<i>Faster</i>	0.026 (0.006)	0.038 (0.010)	0.012 (0.002)	<.0001
<b>Step time (s)</b>				
<i>Slower</i>	0.038 (0.012)	0.040 (0.017)	0.002 (0.003)	0.51
<i>Usual</i>	0.027 (0.007)	0.026 (0.014)	-0.001 (0.003)	0.80
<i>Faster</i>	0.026 (0.007)	0.021 (0.007)	-0.005 (0.003)	0.06
<b>Swing time (s)</b>				
<i>Slower</i>	0.030 (0.008)	0.043 (0.020)	0.012 (0.003)	<.0001
<i>Usual</i>	0.024 (0.004)	0.024 (0.016)	0.000 (0.003)	0.92
<i>Faster</i>	0.023 (0.004)	0.021 (0.008)	-0.003 (0.003)	0.41
<b>Stance time (s)</b>				
<i>Slower</i>	0.050 (0.016)	0.055 (0.025)	0.005 (0.003)	0.12
<i>Usual</i>	0.032 (0.008)	0.031 (0.011)	-0.001 (0.003)	0.67
<i>Faster</i>	0.031 (0.009)	0.027 (0.008)	-0.004 (0.003)	0.22
<b>Double support time (s)</b>				
<i>Slower</i>	0.028 (0.009)	0.036 (0.025)	0.008 (0.003)	0.01
<i>Usual</i>	0.020 (0.003)	0.023 (0.017)	0.004 (0.003)	0.24
<i>Faster</i>	0.017 (0.003)	0.018 (0.007)	0.001 (0.003)	0.73

**Table 12. Change in gait variability between younger and speed-matched older adults from usual to slower and usual to faster.**

<b>Gait Variability</b>	<b>Younger vs. speed-matched older difference in usual to slower change</b>		<b>Younger vs. speed-matched older difference in usual to faster change</b>	
	Difference (SE)	<i>p</i> Value	Difference (SE)	<i>p</i> Value
<b>Step length (m)</b>	0.001 (0.002)	0.72	-0.004 (0.002)	0.06
<b>Step width (m)</b>	-0.005 (0.002)	0.07	-0.008 (0.002)	<.0001
<b>Step time (s)</b>	0.003 (0.003)	0.37	-0.004 (0.003)	0.11
<b>Swing time (s)</b>	0.012 (0.003)	<.0001	-0.003 (0.003)	0.35
<b>Stance time (s)</b>	0.007 (0.004)	0.09	-0.003 (0.003)	0.48
<b>Double support time (s)</b>	0.005 (0.003)	0.14	-0.003 (0.003)	0.43

## **5.0 THE EFFECT OF RHYTHMIC AUDITORY CUEING ON THE SPATIAL AND TEMPORAL GAIT COORDINATION AT DIFFERENT WALKING SPEEDS IN HEALTHY ADULTS**

**Background.** Walk ratio is a simple index for describing the spatial and temporal coordination of gait i.e. walking pattern. To better understand how individuals regulate their walking pattern in order to comply with energy and stability requirements, one possibility is to apply an external constraint (i.e. rhythmic auditory cueing).

**Objective.** The purpose of this study was to examine the impact of rhythmic auditory cueing (metronome) on the walk ratio as an indicator of the spatial and temporal coordination of gait at different walking speeds in healthy adults.

**Study design.** This study was a cross-sectional, observational design.

**Methods.** Forty adults (mean age =  $26.6 \pm 6.0$  years), independent in ambulation, were studied. Gait characteristics were collected using a computerized walkway (GaitMat II™). Step length, step time, cadence and walk ratio were calculated.

**Results.** In the usual walking speed condition, there was no significant difference in spatial and temporal mean gait characteristics and walk ratio between uncued walking, walk ratio =  $0.0064 \pm 0.0007$  and metronome-cued walking, walk ratio =  $0.0064 \pm 0.0007$ ;  $p = 0.791$ . In the slower walking speed condition, participants walked faster and step lengths were longer with metronome-cued walking compared to uncued walking. A higher value of walk ratio at slower speed was observed with metronome-cued walking, walk ratio =  $0.0071 \pm 0.0008$  compared to uncued walking, walk ratio =  $0.0068 \pm 0.0007$ ;  $p < 0.001$ . In the faster walking speed condition, participants walked slower and step lengths were shorter with metronome-cued walking

compared to uncued walking. The walk ratio was less with metronome-cued walking, walk ratio =  $0.0060 \pm 0.0009$  compared to uncued walking, walk ratio =  $0.0062 \pm 0.0009$ ;  $p = 0.005$ .

**Conclusions.** Our findings suggest that a metronome-cued walking, commonly used in gait rehabilitation, may have been detrimental to maintaining the spatial and temporal gait coordination.

**Key words.** Metronome-cued; Walk ratio; Walking pattern; Healthy adults.

## 5.1 INTRODUCTION

The locomotor system for walking results from central and peripheral inputs. The walking system integrates inputs from the cerebellum, the motor cortex, and the basal ganglia, as well as feedback from proprioceptive, visual and vestibular sensors. This dynamic interaction between a central program and feedback mechanisms produces a highly consistent walking pattern.<sup>172-174</sup> Under normal conditions, the spatial and temporal gait parameters appear to remain relatively constant from one step to the next.<sup>1</sup> However, in healthy adults small step to step fluctuations, which can occur as a result of small adaptations to the challenging conditions or non-ideal environments, are usually sufficiently symmetric, rhythmic and stable to prevent falling.<sup>167</sup>

A healthy gait system is characterized by maintaining steady spatial (step length), and temporal (step time) gait parameters and the resulting step speed (i.e. step length/step time) can be viewed as the final outcome which integrates the result of different sensory-motor processes.<sup>32</sup> Therefore, the analysis of walking speed, step length, and step time could theoretically provide insight into the regulation of motor control of the locomotor system.<sup>32</sup> In the late 1960s, it was observed that the ratio between step length and step rate or cadence (called the ‘Walk Ratio’),

did not vary over wide ranges of speed.<sup>175</sup> In fact, the preferred combination of step length and cadence coincides with the minimum energy expenditure, and is optimal in terms of temporal and spatial variability and attentional demand for a given speed.<sup>176-178</sup>

Walk ratio is a simple index for describing the spatial and temporal coordination of gait, i.e. walking pattern.<sup>179</sup> Deviation from the preferential walk ratio during free walking may reveal a degree of abnormal walking patterns. On average, the optimal walk ratio for adults is about 0.0064 (m/steps per min).<sup>179</sup> Aging or neuro-degenerative diseases such as Parkinson's disease and multiple sclerosis can modify the walking pattern and induce a smaller walk ratio.<sup>180-182</sup> The walk ratio, which incorporates both temporal and spatial gait characteristics, can be a useful integrated measure of the neuromotor control of gait. As such, the walk ratio could be important in the evaluation of pathological and aging walking patterns.

In order to better understand how individuals regulate their walking pattern in order to comply with energy and stability requirements,<sup>172</sup> one possibility is to apply an external constraint (i.e. external auditory cueing) and to examine the resulting change in the walk ratio. The synchronization of body movements to rhythmic auditory cueing is a remarkable ability of the human brain.<sup>150,151</sup> Rhythm is defined as the time-based pattern of music or sound that consists of perceptible groupings of notes, beats, accents, and phrases. This powerful connection between rhythm and locomotion has had positive effects for improving spatio-temporal features of gait of patients with neurological disorders including Parkinson disease, stroke and hemiparesis.<sup>11-14</sup> For instance, in patients with Parkinson's disease synchronizing steps with rhythmic auditory cueing significantly improved walking speed, stride length and cadence.<sup>15</sup>

However, it is difficult to completely interpret the influence of rhythmic auditory cueing on the neuromotor control of abnormal gait without first understanding the induced effects in healthy adults in the absence of aging and pathology at different walking speeds. Therefore, the purpose of this study was to examine the impact of rhythmic auditory cueing (metronome) on the walk ratio as an indicator of the neuromotor control of gait at different walking speeds in healthy adults. Our hypothesis was that the walk ratio will deviate from the optimal value at slower and faster speeds compared to usual preferred walking speed. With changing speed (i.e. walking slower or faster than usual preferred speed), the metronome-cued walking would facilitate a consistent ratio between step length and cadence.

## **5.2 METHODS**

### **5.2.1 Participants**

Forty healthy adults were included in the study. They were recruited through fliers posted throughout the University of Pittsburgh. The participants were between the ages of 18 and 50, and had no diagnosed neuromuscular, cardiopulmonary, or orthopedic conditions that would affect walking. They were first screened over the phone to determine initial eligibility. Subjects who passed the phone screen were scheduled for a one-hour clinic visit which included a physical exam (range of motion and muscle testing) to determine final eligibility, followed by measurement of gait characteristics using a computerized walkway.

This study was approved by the University of Pittsburgh Institutional Review Board, and all participants provided informed consent prior to participation.

### **5.2.2 Procedure**

Spatial and temporal gait characteristics were collected using a computerized walkway (GaitMat II™) (EQ Inc, Chalfont, PA).<sup>37</sup> The GaitMat II is an automated gait analysis system, based on the opening and closing of pressure sensitive switches on the walkway that are displayed on the computer screen as footprints when the participant walks. The GaitMat II provides a temporal resolution of 5 ms and a spatial resolution of 15 mm in both the longitudinal and transverse directions. The GaitMat II was approximately 12 meters in length. The initial and final 2 meters were inactive sections to allow for acceleration and deceleration of the participant. The middle 8 meters were active and used for data collection. The reliability and validity of the computerized walkway has been established for quantification of the spatial and temporal mean gait characteristics for a variety of populations including children,<sup>59</sup> healthy young adults,<sup>60</sup> healthy older adults,<sup>7,60</sup> and individuals with Parkinson's disease<sup>61</sup> and Huntington disease.<sup>62</sup>

#### **5.2.2.1 Uncued walking**

Spatial and temporal gait data were collected at three walking speed conditions. Each participant completed two practice walks the length of the walkway for each walking speed condition to become familiar to walking on mat. Each walk was considered one pass. After practice trials, four passes were collected at each walking speed condition (usual, slower and faster). For usual uncued walking speed: participants were instructed to walk at a pace that represented their usual walking speed as they completed various tasks throughout their daily routines. For slower uncued walking speed: participants were instructed to walk as slowly as they could without



stopping. For faster uncued walking speed: participants were asked to walk as fast as they could without running or putting themselves at risk of falling.

#### **5.2.2.2 Metronome-cued walking**

Each participant then completed two practice walks the length of the walkway for each walking speed condition with the metronome-cued to become familiar to walking on the mat with the metronome-cued. Instructions were given to start walking in time to the beat of the metronome-cued along the walkway for each walking speed condition (usual, slower and faster).

The rhythmic auditory cueing was a metronome beat (Metronome plus App for iphone) connected through Bluetooth to speakers positioned adjacent to the walkway, with sound volume set at an “easily audible” level for each participant. The mean cadence for each participant was calculated for usual, slower and faster walking speeds. Metronome-cued was set at a tempo matched to individual mean cadence for each walking speed.

#### **5.2.3 Data processing**

GaitMat II data were inspected and cleaned for half foot-prints (footprints that occur at the beginning and the end of the mat) and extraneous points. Mean step length, step time, cadence and walk ratio were computed for all steps over all passes. Step length was defined as the distance between 2 consecutive footprints, measured from the heel of one footprint to the heel of the next footprint and was recorded in meters.<sup>7</sup> Step time was defined as the time between initial foot-floor contact of one foot to the initial foot-floor contact of the contralateral side, recorded in

seconds.<sup>7</sup> Cadence was defined as the number of steps per minute (steps/min). Walk ratio (m/steps/min) was determined by dividing the step length (m) by cadence (steps/min).<sup>179</sup>

#### **5.2.4 Statistical analysis**

All statistical analyses were conducted with SAS<sup>®</sup> version 9.3 (SAS Institute, Inc., Cary, North Carolina). We computed appropriate descriptive statistics to describe the study sample. We fit a mixed linear model using the SAS<sup>®</sup> MIXED procedure with each measure of spatial and temporal mean gait characteristics and walk ratio as the response variable; walking condition (uncued and metronome-cued), walking speed (usual, slower, faster), and walking condition  $\times$  walking speed interaction as fixed effects of interest; and a participant random effect to account for the same participants performing under multiple conditions and the resulting stochastic nonindependence of observations. Appropriate contrasts were constructed to compare walking condition within each walking speed; and compare walking speed within each walking condition. To ensure the soundness of our statistical approach, we examined the residuals from the mixed models and constructed normal probability plots to determine if they were normally distributed.

## **5.3 RESULTS**

### **5.3.1 Participant characteristics**

Forty healthy adults were included in the study: 10 males and 30 females, with a mean (standard deviation) age of 26.6 (6.0) years, body height = 168.4 (8.3) cm and body weight = 66.4 (12.4) kg. All participants changed their speeds appropriately for the different walking speed conditions during uncued and metronome-cued walking, all  $p < .0001$ .

### **5.3.2 The impact of rhythmic auditory cueing on spatial and temporal mean characteristics at different walking speed**

Means and standard deviation of the spatial and temporal gait parameters during uncued and metronome-cued walking at each walking speed are presented in Table 13. In the usual walking speed condition, there was no difference in spatial and temporal mean gait characteristics and walk ratio between uncued and metronome-cued walking.

In the slower walking speed condition, participants walked faster step lengths were longer with metronome-cued compared to uncued walking. Mean step time and cadence did not differ between uncued and metronome-cued walking. A higher value for walk ratio at slower speed was observed with metronome-cued compared to uncued walking (Table 13).

In the faster walking speed condition, participants walked slower and step lengths were shorter with metronome-cued compared to uncued walking. Mean step time did not differ between uncued and metronome-cued walking. Mean cadence reduced with metronome-cued

compared to uncued walking. The walk ratio was lower with metronome-cued compared to uncued walking (Table 13).

Fig. 5 illustrates walk ratio data at individual level. At usual speed, few individuals demonstrate large changes in the walk ratio with metronome-cued compared to uncued walking. At slower and faster pace, individuals were more likely to demonstrate a change in walk ratio between uncued and metronome-cued walking.

## 5.4 DISCUSSION

We set out to examine the impact of metronome cueing on walk ratio during usual speed and in changed speed conditions. We observed that walk ratio remained constant between uncued and metronome-cued walking at usual speed. Our findings confirmed what previous studies had suggested that under normal conditions, there is consistent relation between step length and cadence which is relates to the minimization of energy consumption per unit distance in healthy adults.<sup>176,177</sup> Walking at self-selected speed in a stable environment with minimal attention is controlled by the basal ganglia through its connections to frontal cortical regions.<sup>183-185</sup> It has been suggested that interactions between basal ganglia and supplementary motor area could provide the correct step length and cadence for optimal efficiency which in turn allows for the walking of self-selected speed in automatic mode.<sup>186</sup> In contrast to what we hypothesized, in the slower walking speed condition, walk ratio was higher with metronome-cued compared to uncued walking. In the faster walking speed condition, walk ratio was lower with metronome-cued compared to uncued walking. One possible reason is that metronome cueing disrupts gait

timing by increasing the attentional demand of walking at non-ideal speeds conditions voluntary induced such as slower and faster speeds. Synchronizing movement with rhythmic auditory cued requires complex supraspinal mechanisms. Such synchronization has been reported to induce increased neuronal activity in sensorimotor cortex, supplementary motor area, premotor cortex, inferior parietal cortex, basal ganglia and cerebellum.<sup>187</sup>

In evaluating how well mean cadence matched cue frequency, we measured “frequency-matching” or how well mean cadence matched metronome-cued frequency. Metronome-cued walking provoked a significant decrease in mean cadence values during faster speed compared to uncued and a small increase in mean cadence values during slower speed compared to uncued, indicating that footfalls were not fully synchronized with metronome-cued. However, we did not measure synchronization of footfalls to individual metronome beats. A recent study in healthy young adults found that consecutive footfalls were not fully synchronized with metronome beats.<sup>188</sup> Future investigation needs to examine synchronization of footfalls with metronome-cued in healthy older and young adults, that would further our insight when evaluating effects of rhythmic auditory cueing on gait.

#### **5.4.1 Study limitations**

The findings of this study should be interpreted in light of some limitations. First, participants did not walk at a set speed. Spatial and temporal gait parameters were examined during self-selected over-ground walking, where subjects were directed to walk “slower”, “usual” and “faster”. The most common approach to control for walking speed is through treadmill walking. However, the treadmill itself acts as an external cue, which may regulate gait. As a result, if

individuals are subjected to auditory stimuli while walking on a treadmill, it is possible they have to adapt their gait to different constraints, i.e., the auditory and the speed constraints. In addition, our sample consisted of healthy young and middle age adults so the findings cannot be generalized to community dwelling older adults or to clinical populations.

## **5.5 CONCLUSION**

Our findings suggest that a metronome-cue, commonly used in gait rehabilitation, may have been detrimental to the spatio-temporal coordination of gait. It is possible that metronome cue disrupts gait timing by increasing the attentional demand of walking at non-ideal speeds such as slower and faster speeds in healthy adults.

**Table 13. Comparison of mean gait characteristics between uncued and metronome-cued walking at different walking speeds.**

Mean gait characteristics	Slower			Usual			Faster		
	Uncued	Metronome-cued	<i>P</i> value	Uncued	Metronome-cued	<i>P</i> value	Uncued	Metronome-cued	<i>P</i> value
<b>Gait speed (m/s)</b>	0.90 (0.17)	0.97 (0.19)	0.003	1.29 (0.19)	1.28 (0.20)	0.738	1.76 (0.22)	1.61 (0.22)	<.0001
<b>Step length (m)</b>	0.60 (0.06)	0.64 (0.07)	<.0001	0.70 (0.06)	0.70 (0.07)	0.663	0.81 (0.08)	0.76 (0.08)	<.0001
<b>Step time (s)</b>	0.68 (0.08)	0.67 (0.08)	0.287	0.55 (0.05)	0.55 (0.05)	0.877	0.46 (0.04)	0.47 (0.04)	0.190
<b>Cadence (steps/min)</b>	89.2 (10.3)	90.5 (10.8)	0.356	109.9 (10.3)	109.8 (10.6)	0.898	130.7 (12.9)	127.8 (12.4)	0.0276
<b>Walk ratio (m/steps per min)</b>	0.0068 (0.0007) [0.0053, 0.0084]	0.0071 (0.0008) [0.0055, 0.0089]	<.0001	0.0064 (0.0007) [0.0052, 0.0082]	0.0064 (0.0007) [0.0049, 0.0082]	0.791	0.0062 (0.0009) [0.0044, 0.0079]	0.0060 (0.0009) [0.0042, 0.0073]	0.005

Note: Values are mean (standard deviation) [range] unless otherwise noted.

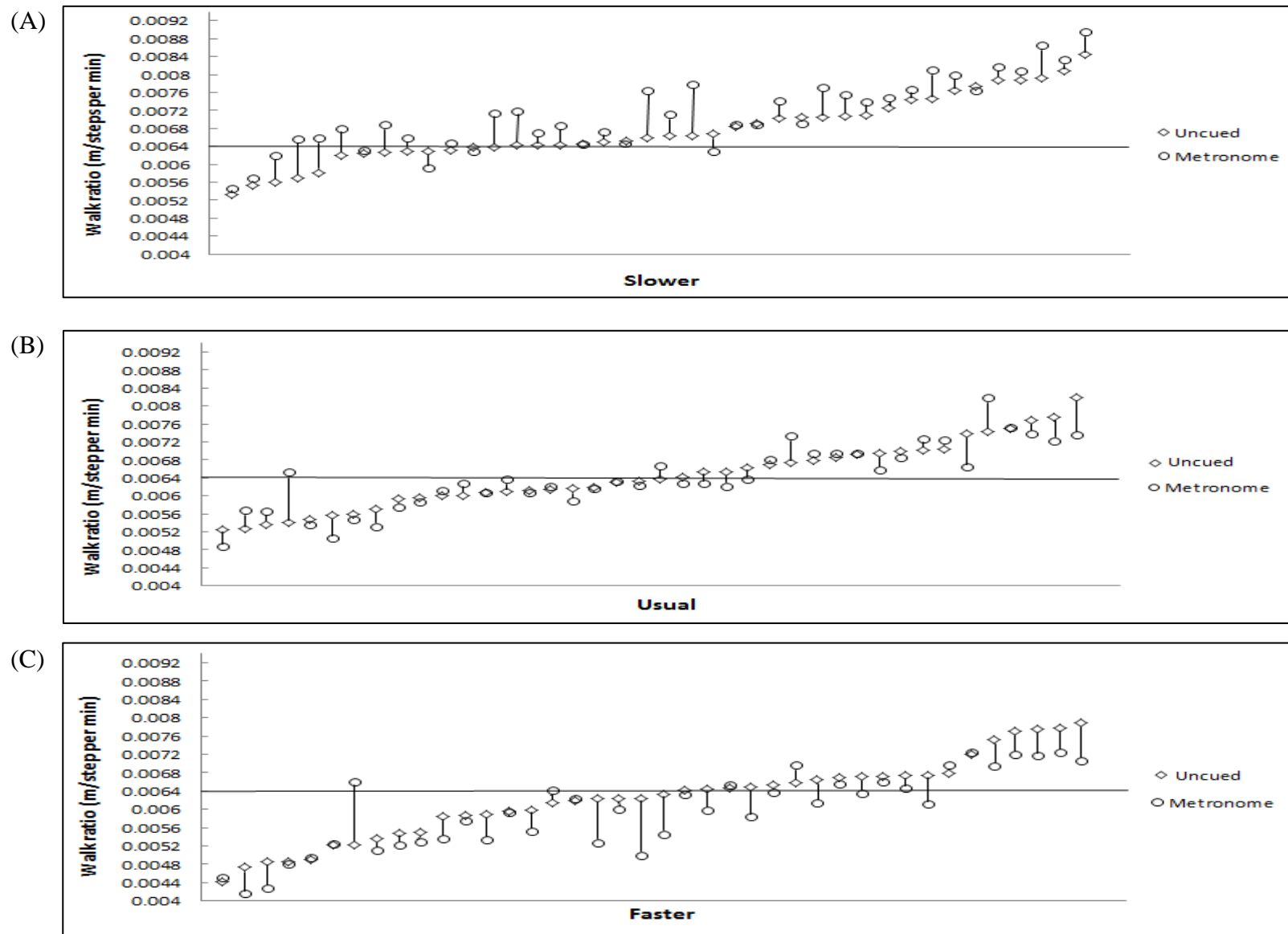


Figure 5. The impact of metronome-cued walking on individual walk ratio at different walking speeds (A) slower, (B) usual and (C) faster. The bold horizontal is presented the optimized walk ratio value, (walk ratio = 0.0064).



## **6.0 CLINICAL SIGNIFICANCE AND DIRECTION OF FUTURE RESEARCH**

This study investigated spatial and temporal gait characteristics in healthy younger and older adults. The major aim was to advance our knowledge about timing and coordination of gait by investigating the impact of potential factors such as aging, challenging walking conditions (slower and faster speeds) and external rhythmic cueing (metronome) that could impact the spatial and temporal gait characteristics.

The findings of our first study support our hypothesis that younger adults are more consistent from time to time and fluctuate less over time compared to older adults. Therefore, our findings suggest that in older adults, some age-related decline in the organization and stability of the gait cycle is expected, which may be indicative of the overall health and control of the locomotor system. Furthermore, the current findings may suggest the use of spatial and temporal gait variability as a valuable measure for assessing the stability of the locomotor system.

### **6.1 CONSISTENCY OF GAIT VARIABILITY**

Little is known about the “consistency” of gait variability; are individuals consistently variable or will their variability change in magnitude from session to session? It would benefit us to know whether our participants were stable (consistent) or unstable (inconsistent) in their level of

spatial and temporal gait variability. Our first study showed that not all older adults vary the same in their gait variability over time. Bland Altman plots showed that in older adults greater gait variability was associated with a greater difference in gait variability from visit 1 to visit 2 (i.e. greater inconsistency). However, many of the older adults with low gait variability had a small difference in gait variability from session to session (i.e. consistent gait variability) which is similar to the younger participants. It is possible that age-related declines in both physical and cognitive functioning might contribute to greater inconsistency of gait variability in some of older adults in our study over time.

Future longitudinal study should further investigate inconsistency of gait variability as a potential early indicator of a decline in mobility. For example, measuring gait variability at more frequent time intervals whether it's daily or hourly to see if this inconsistency in gait variability is a true phenomenon and may be an informative characteristic of the individual which could be a marker of early decline in the locomotor control and stability and not simply an indicator of a measurement error. In this sense, it is also important to investigate meaningful change of spatial and temporal gait variability. Brach et al. has estimated meaningful change of gait variability in 241 community older adults based on annual follow up analyses.<sup>41</sup> However, meaningful change of spatial and temporal gait variability over short time and in clinical population is unclear.

## **6.2 IS HIGHER GAIT VARIABILITY NECESSARILY A NEGATIVE FACTOR DURING SLOWER WALKING IN OLDER ADULTS?**

The influence of underlying health on gait variability during slower walking is unknown. The results of this cross-sectional study using independent older adults suggest that increase gait variability is independent of slower walking speed. The increased gait variability demonstrated by older adults at slower walking speed may be related to underlying subclinical pathology in important neural locomotor regions, and not simply a manifestation of slower walking speed.

Functional magnetic resonance imaging studies have shown increased activity in the neurons in the motor cortex during challenging walking (i.e. stepping over obstacle) and when adjusting posture.<sup>189,190</sup> Other researchers have suggested that cerebral cortex becomes more involved in locomotor control with increasing effort and attentional demands. Consequently, it would appear from these studies that the basal ganglia and brainstem may be able to control unconstrained steady state locomotion with minimal cortical activity (i.e. preferred usual walking), although some background activation is still required to adapt to any unexpected environmental demand.<sup>184,185</sup> However, for increasingly complex walking where attentional demand is required, greater cortical control appeared necessary. Future longitudinal studies are needed to determine if changes in gait variability on challenging gait conditions predicts future mobility disability in higher functioning older adults with near normal gait.

## **6.3 MECHANISM OF SPATIAL AND TEMPORAL GAIT VARIABILITY**

Gait variability is not a single entity, but is derived from a range of spatio-temporal

characteristics. Spatial and temporal gait variability may provide independent information of locomotion and should not be considered equivalent descriptor of gait variability. The results of our second study showed significant change in gait variability in all temporal gait characteristics from usual to slower pace walking (i.e. greater impact) in older adults. Walking slowly might require greater attention, due to reduced gait automaticity and higher cortical demand. Previous study suggest that stronger associations between executive function/attention and temporal versus spatial variability measures may be due to the timing component of the cognitive tests.<sup>86</sup> Underlying mechanisms of spatial and temporal gait variability during challenging walking are still unclear.

Future studies are needed to investigate the impact of challenging walking conditions on different types of spatial and temporal gait variability independently because if underlying mechanisms of variable gait are better understood, then distinct interventions can be designed to address specific deficiencies. It is possible that individually designed therapeutic exercise programs based on the type of gait variability could result in greater improvements in walking function and overall mobility.

## **6.4 LIMITATIONS**

There are several limitations in our studies that need to be acknowledged. First, gait variability was collected during intermittent walks with a limited numbers of passes. Testing protocol can impact the reliability of gait variability. Recently, Galna et al. suggested using a continuous walking protocol instead of short intermittent walks with no fewer than 30 steps to improve the

reliability of gait variability.<sup>120</sup> However, the purpose of our study was to compare the reliability of gait variability between younger and older adults, as commonly measured over short distances, and not to maximize the reliability estimate of gait variability. Second, participants did not walk at a set speed. Spatial and temporal gait parameters were examined during self-selected over-ground walking, where subjects were directed to walk “slower”, “usual” and “faster”. The most common approach to control for walking speed is through treadmill walking. However, the treadmill acts as an external cue, which may regulate gait. Another limitation is that older adults were part of a group from a previous study and therefore the sample could not be and therefore the sample could not be properly selected. Finally, the results of our study applied only for community dwelling older adults and healthy younger adults, and it is difficult to extrapolate the discussion for clinical populations.

## **6.5 CONCLUSION**

In conclusion, this investigation found evidence that younger adults had greater test-retest reliability and smaller MDC of spatial and temporal gait variability compared to older adults. In older adults, walking slowly is more challenging to the motor control of gait and may be more sensitive to age-related declines in gait than usual and faster speed walks. Finally, a metronome cue, commonly used in gait rehabilitation, may actually be detrimental to maintaining the spatial and temporal gait coordination. It is possible that metronome cues disrupt gait timing by increasing the attentional demand of walking at non-ideal speeds such as slower and faster speeds.

## BIBLIOGRAPHY

1. Hausdorff JM. Gait variability: methods, modeling and meaning. *J Neuroeng Rehabil.* 2005;2:19.
2. Brach JS, Berthold R, Craik R, et al. Gait variability in community-dwelling older adults. *J Am Geriatr Soc.* 2001;49:1646-1650.
3. Brach JS, McGurl D, Wert D, et al. Validation of a measure of smoothness of walking. *J Gerontol A Biol Sci Med Sci.* 2011;66:136-141.
4. Wert DM, Brach J, Perera S, et al. Gait biomechanics, spatial and temporal characteristics, and the energy cost of walking in older adults with impaired mobility. *Phys Ther.* 2010;90:977-985.
5. VanSwearingen JM, Perera S, Brach JS, et al. A randomized trial of two forms of therapeutic activity to improve walking: effect on the energy cost of walking. *J Gerontol A Biol Sci Med Sci.* 2009;64:1190-1198.
6. Lord S, Howe T, Greenland J, et al. Gait variability in older adults: a structured review of testing protocol and clinimetric properties. *Gait Posture.* 2011;34:443-450.
7. Brach JS, Perera S, Studenski S, et al. The reliability and validity of measures of gait variability in community-dwelling older adults. *Arch Phys Med Rehabil.* 2008;89:2293-2296.
8. Hars M, Herrmann FR, Trombetti A. Reliability and minimal detectable change of gait variables in community-dwelling and hospitalized older fallers. *Gait Posture.* 2013;38:1010-1014.
9. Ko SU, Hausdorff JM, Ferrucci L. Age-associated differences in the gait pattern changes of older adults during fast-speed and fatigue conditions: results from the Baltimore longitudinal study of ageing. *Age Ageing.* 2010;39:688-694.
10. Nascimbeni A, Minichillo M, Salatino A, et al. Gait attentional load at different walking speeds. *Gait Posture.* 2015;41:304-306.

11. Nascimento LR, de Oliveira CQ, Ada L, et al. Walking training with cueing of cadence improves walking speed and stride length after stroke more than walking training alone: a systematic review. *J Physiother.* 2015;61:10-15.
12. Pelton TA, Johannsen L, Huiya C, et al. Hemiparetic stepping to the beat: asymmetric response to metronome phase shift during treadmill gait. *Neurorehabil Neural Repair.* 2010;24:428-434.
13. Roerdink M, Lamoth CJ, van Kordelaar J, et al. Rhythm perturbations in acoustically paced treadmill walking after stroke. *Neurorehabil Neural Repair.* 2009;23:668-678.
14. Suteerawattananon M, Morris GS, Etnyre BR, et al. Effects of visual and auditory cues on gait in individuals with Parkinson's disease. *J Neurol Sci.* 2004;219:63-69.
15. Lim I, van Wegen E, de Goede C, et al. Effects of external rhythmical cueing on gait in patients with Parkinson's disease: a systematic review. *Clin Rehabil.* 2005;19:695-713.
16. Newell KM, Corcos DM. *Variability and motor control.* Champaign IL: Human Kinetics Publishers; 1993.
17. Lipsitz LA. Physiological complexity, aging, and the path to frailty. *Sci Aging Knowledge Environ.* 2004;2004:pe16.
18. Stergiou N, Decker LM. Human movement variability, nonlinear dynamics, and pathology: is there a connection? *Hum Mov Sci.* 2011;30:869-888.
19. Stergiou N, Harbourne R, Cavanaugh J. Optimal movement variability: a new theoretical perspective for neurologic physical therapy. *J Neurol Phys Ther.* 2006;30:120-129.
20. Bernshstein NA. *The co-ordination and regulation of movements.* [1st English ed. Oxford, New York,; Pergamon Press; 1967.
21. Gabel A, Nayak US. The effect of age on variability in gait. *J Gerontol.* 1984;39:662-666.
22. Hausdorff JM, Purdon PL, Peng CK, et al. Fractal dynamics of human gait: stability of long-range correlations in stride interval fluctuations. *J Appl Physiol* (1985). 1996;80:1448-1457.
23. Herman T, Giladi N, Gurevich T, et al. Gait instability and fractal dynamics of older adults with a "cautious" gait: why do certain older adults walk fearfully? *Gait Posture.* 2005;21:178-185.
24. Hollman JH, Kovash FM, Kubik JJ, et al. Age-related differences in spatiotemporal markers of gait stability during dual task walking. *Gait Posture.* 2007;26:113-119.

25. Maki BE. Gait changes in older adults: predictors of falls or indicators of fear. *J Am Geriatr Soc.* 1997;45:313-320.
26. Baltadjieva R, Giladi N, Gruendlinger L, et al. Marked alterations in the gait timing and rhythmicity of patients with de novo Parkinson's disease. *Eur J Neurosci.* 2006;24:1815-1820.
27. Webster KE, Merory JR, Wittwer JE. Gait variability in community dwelling adults with Alzheimer disease. *Alzheimer Dis Assoc Disord.* 2006;20:37-40.
28. Hausdorff JM, Rios DA, Edelberg HK. Gait variability and fall risk in community-living older adults: a 1-year prospective study. *Arch Phys Med Rehabil.* 2001;82:1050-1056.
29. Montero-Odasso M, Muir SW, Hall M, et al. Gait variability is associated with frailty in community-dwelling older adults. *J Gerontol A Biol Sci Med Sci.* 2011;66:568-576.
30. Brach JS, Berlin JE, VanSwearingen JM, et al. Too much or too little step width variability is associated with a fall history in older persons who walk at or near normal gait speed. *J Neuroeng Rehabil.* 2005;2:21.
31. Brach JS, Studenski SA, Perera S, et al. Gait variability and the risk of incident mobility disability in community-dwelling older adults. *J Gerontol A Biol Sci Med Sci.* 2007;62:983-988.
32. Hausdorff JM. Gait dynamics, fractals and falls: finding meaning in the stride-to-stride fluctuations of human walking. *Hum Mov Sci.* 2007;26:555-589.
33. Whittle M. *Gait analysis : an introduction.* 4th ed. Edinburgh ; New York: Butterworth-Heinemann; 2007.
34. Chambers HG, Sutherland DH. A practical guide to gait analysis. *J Am Acad Orthop Surg.* 2002;10:222-231.
35. Huxham F, Gong J, Baker R, et al. Defining spatial parameters for non-linear walking. *Gait Posture.* 2006;23:159-163.
36. Trew M, Everett T. *Human movement : an introductory text.* 5th ed. Edinburgh ; New York: Elsevier/Churchill Livingstone; 2005.
37. Craik R, Oatis CA. *Gait analysis : theory and application.* St. Louis: Mosby; 1995.
38. Rueterbories J, Spaich EG, Larsen B, et al. Methods for gait event detection and analysis in ambulatory systems. *Med Eng Phys.* 2010;32:545-552.



39. Chau T, Young S, Redekop S. Managing variability in the summary and comparison of gait data. *J Neuroeng Rehabil.* 2005;2:22.
40. Brach JS, Studenski S, Perera S, et al. Stance time and step width variability have unique contributing impairments in older persons. *Gait Posture.* 2008;27:431-439.
41. Brach JS, Perera S, Studenski S, et al. Meaningful change in measures of gait variability in older adults. *Gait Posture.* 2010;31:175-179.
42. Martin KL, Blizzard L, Wood AG, et al. Cognitive function, gait, and gait variability in older people: a population-based study. *J Gerontol A Biol Sci Med Sci.* 2013;68:726-732.
43. Mbourou GA, Lajoie Y, Teasdale N. Step length variability at gait initiation in elderly fallers and non-fallers, and young adults. *Gerontology.* 2003;49:21-26.
44. Owings TM, Grabiner MD. Step width variability, but not step length variability or step time variability, discriminates gait of healthy young and older adults during treadmill locomotion. *J Biomech.* 2004;37:935-938.
45. Beauchet O, Allali G, Annweiler C, et al. Gait variability among healthy adults: low and high stride-to-stride variability are both a reflection of gait stability. *Gerontology.* 2009;55:702-706.
46. Hollman JH, Childs KB, McNeil ML, et al. Number of strides required for reliable measurements of pace, rhythm and variability parameters of gait during normal and dual task walking in older individuals. *Gait Posture.* 2010;32:23-28.
47. Moe-Nilssen R, Aaslund MK, Hodt-Billington C, et al. Gait variability measures may represent different constructs. *Gait Posture.* 2010;32:98-101.
48. Hausdorff JM, Edelberg HK, Mitchell SL, et al. Increased gait unsteadiness in community-dwelling elderly fallers. *Arch Phys Med Rehabil.* 1997;78:278-283.
49. Paterson KL, Lythgo ND, Hill KD. Gait variability in younger and older adult women is altered by overground walking protocol. *Age Ageing.* 2009;38:745-748.
50. Baumgartner TA. *Measurement for evaluation in physical education and exercise science.* 8th ed. Boston: McGraw-Hill; 2007.
51. Hopkins WG. Measures of reliability in sports medicine and science. *Sports Med.* 2000;30:1-15.
52. Bland JM, Altman DG. Measurement error. *BMJ.* 1996;313:744.

53. Bland M. *An introduction to medical statistics*. 2nd ed. Oxford ; New York: Oxford University Press; 1995.
54. Lee JA, Cho SH, Lee YJ, et al. Portable activity monitoring system for temporal parameters of gait cycles. *J Med Syst*. 2010;34:959-966.
55. Beauchet O, Herrmann FR, Grandjean R, et al. Concurrent validity of SMTEC footswitches system for the measurement of temporal gait parameters. *Gait Posture*. 2008;27:156-159.
56. Hartmann A, Murer K, de Bie RA, et al. Reproducibility of spatio-temporal gait parameters under different conditions in older adults using a trunk tri-axial accelerometer system. *Gait Posture*. 2009;30:351-355.
57. Hartmann A, Luzi S, Murer K, et al. Concurrent validity of a trunk tri-axial accelerometer system for gait analysis in older adults. *Gait Posture*. 2009;29:444-448.
58. Najafi B, Helbostad JL, Moe-Nilssen R, et al. Does walking strategy in older people change as a function of walking distance? *Gait Posture*. 2009;29:261-266.
59. Thorpe DE, Dusing SC, Moore CG. Repeatability of temporospatial gait measures in children using the GAITRite electronic walkway. *Arch Phys Med Rehabil*. 2005;86:2342-2346.
60. Menz HB, Latt MD, Tiedemann A, et al. Reliability of the GAITRite walkway system for the quantification of temporo-spatial parameters of gait in young and older people. *Gait Posture*. 2004;20:20-25.
61. Nelson AJ, Zwick D, Brody S, et al. The validity of the GaitRite and the Functional Ambulation Performance scoring system in the analysis of Parkinson gait. *NeuroRehabilitation*. 2002;17:255-262.
62. Rao AK, Quinn L, Marder KS. Reliability of spatiotemporal gait outcome measures in Huntington's disease. *Mov Disord*. 2005;20:1033-1037.
63. Verghese J, Wang C, Lipton RB, et al. Quantitative gait dysfunction and risk of cognitive decline and dementia. *J Neurol Neurosurg Psychiatry*. 2007;78:929-935.
64. Hausdorff JM, Nelson ME, Kaliton D, et al. Etiology and modification of gait instability in older adults: a randomized controlled trial of exercise. *J Appl Physiol* (1985). 2001;90:2117-2129.
65. Ijmker T, Lamoth CJ. Gait and cognition: the relationship between gait stability and variability with executive function in persons with and without dementia. *Gait Posture*. 2012;35:126-130.

66. Hausdorff JM, Schweiger A, Herman T, et al. Dual-task decrements in gait: contributing factors among healthy older adults. *J Gerontol A Biol Sci Med Sci*. 2008;63:1335-1343.
67. Springer S, Giladi N, Peretz C, et al. Dual-tasking effects on gait variability: the role of aging, falls, and executive function. *Mov Disord*. 2006;21:950-957.
68. Montero-Odasso M, Wells JL, Borrie MJ, et al. Can cognitive enhancers reduce the risk of falls in older people with mild cognitive impairment? A protocol for a randomised controlled double blind trial. *BMC Neurol*. 2009;9:42.
69. Trombetti A, Hars M, Herrmann FR, et al. Effect of music-based multitask training on gait, balance, and fall risk in elderly people: a randomized controlled trial. *Arch Intern Med*. 2011;171:525-533.
70. Menz HB, Lord SR, Fitzpatrick RC. Acceleration patterns of the head and pelvis when walking are associated with risk of falling in community-dwelling older people. *J Gerontol A Biol Sci Med Sci*. 2003;58:M446-452.
71. Hausdorff JM, Cudkowicz ME, Firtion R, et al. Gait variability and basal ganglia disorders: stride-to-stride variations of gait cycle timing in Parkinson's disease and Huntington's disease. *Mov Disord*. 1998;13:428-437.
72. Hausdorff JM. Gait dynamics in Parkinson's disease: common and distinct behavior among stride length, gait variability, and fractal-like scaling. *Chaos*. 2009;19:026113.
73. Hausdorff JM, Lertratanakul A, Cudkowicz ME, et al. Dynamic markers of altered gait rhythm in amyotrophic lateral sclerosis. *J Appl Physiol* (1985). 2000;88:2045-2053.
74. Socie MJ, Sosnoff JJ. Gait variability and multiple sclerosis. *Mult Scler Int*. 2013;2013:645197.
75. Beauchet O, Dubost V, Herrmann FR, et al. Stride-to-stride variability while backward counting among healthy young adults. *J Neuroeng Rehabil*. 2005;2:26.
76. Dubost V, Kressig RW, Gonthier R, et al. Relationships between dual-task related changes in stride velocity and stride time variability in healthy older adults. *Hum Mov Sci*. 2006;25:372-382.
77. Dubost V, Annweiler C, Aminian K, et al. Stride-to-stride variability while enumerating animal names among healthy young adults: result of stride velocity or effect of attention-demanding task? *Gait Posture*. 2008;27:138-143.
78. Verghese J, Robbins M, Holtzer R, et al. Gait dysfunction in mild cognitive impairment syndromes. *J Am Geriatr Soc*. 2008;56:1244-1251.

79. Zimmerman ME, Lipton RB, Pan JW, et al. MRI- and MRS-derived hippocampal correlates of quantitative locomotor function in older adults. *Brain Res.* 2009;1291:73-81.
80. Kurz MJ, Stergiou N. The spanning set indicates that variability during the stance period of running is affected by footwear. *Gait Posture.* 2003;17:132-135.
81. Goldberger AL, Amaral LA, Hausdorff JM, et al. Fractal dynamics in physiology: alterations with disease and aging. *Proc Natl Acad Sci U S A.* 2002;99 Suppl 1:2466-2472.
82. McAndrew PM, Dingwell JB, Wilken JM. Walking variability during continuous pseudo-random oscillations of the support surface and visual field. *J Biomech.* 2010;43:1470-1475.
83. Dobbs RJ, Charlett A, Bowes SG, et al. Is this walk normal? *Age Ageing.* 1993;22:27-30.
84. Hausdorff JM. Stride variability: beyond length and frequency. *Gait Posture.* 2004;20:304; author reply 305.
85. Beauchet O, Dubost V, Herrmann F, et al. Relationship between dual-task related gait changes and intrinsic risk factors for falls among transitional frail older adults. *Aging Clin Exp Res.* 2005;17:270-275.
86. Callisaya ML, Blizzard L, Schmidt MD, et al. Gait, gait variability and the risk of multiple incident falls in older people: a population-based study. *Age Ageing.* 2011;40:481-487.
87. Rosano C, Brach J, Studenski S, et al. Gait variability is associated with subclinical brain vascular abnormalities in high-functioning older adults. *Neuroepidemiology.* 2007;29:193-200.
88. Hausdorff JM, Lowenthal J, Herman T, et al. Rhythmic auditory stimulation modulates gait variability in Parkinson's disease. *Eur J Neurosci.* 2007;26:2369-2375.
89. Hausdorff JM, Mitchell SL, Firtion R, et al. Altered fractal dynamics of gait: reduced stride-interval correlations with aging and Huntington's disease. *J Appl Physiol* (1985). 1997;82:262-269.
90. Dingwell JB, Cavanagh PR. Increased variability of continuous overground walking in neuropathic patients is only indirectly related to sensory loss. *Gait Posture.* 2001;14:1-10.
91. Papadakis NC, Christakis DG, Tzagarakis GN, et al. Gait variability measurements in lumbar spinal stenosis patients: part B. Preoperative versus postoperative gait variability. *Physiol Meas.* 2009;30:1187-1195.

92. Kang HG, Dingwell JB. Separating the effects of age and walking speed on gait variability. *Gait Posture*. 2008;27:572-577.
93. Ilg W, Golla H, Thier P, et al. Specific influences of cerebellar dysfunctions on gait. *Brain*. 2007;130:786-798.
94. Nutt JG, Marsden CD, Thompson PD. Human walking and higher-level gait disorders, particularly in the elderly. *Neurology*. 1993;43:268-279.
95. Maki BE, Holliday PJ, Topper AK. A prospective study of postural balance and risk of falling in an ambulatory and independent elderly population. *J Gerontol*. 1994;49:M72-84.
96. Hamacher D, Singh NB, Van Dieen JH, et al. Kinematic measures for assessing gait stability in elderly individuals: a systematic review. *J R Soc Interface*. 2011;8:1682-1698.
97. McGibbon CA. Toward a better understanding of gait changes with age and disablement: neuromuscular adaptation. *Exerc Sport Sci Rev*. 2003;31:102-108.
98. Winter DA, Patla AE, Frank JS, et al. Biomechanical walking pattern changes in the fit and healthy elderly. *Phys Ther*. 1990;70:340-347.
99. Prince F, Corriveau H, Hébert R, et al. Gait in the elderly. *Gait & Posture*. 5:128-135.
100. Himann JE, Cunningham DA, Rechnitzer PA, et al. Age-related changes in speed of walking. *Med Sci Sports Exerc*. 1988;20:161-166.
101. Hageman PA, Blanke DJ. Comparison of gait of young women and elderly women. *Phys Ther*. 1986;66:1382-1387.
102. Ferrucci L, Baldasseroni S, Bandinelli S, et al. Disease severity and health-related quality of life across different chronic conditions. *J Am Geriatr Soc*. 2000;48:1490-1495.
103. Studenski S, Perera S, Wallace D, et al. Physical performance measures in the clinical setting. *J Am Geriatr Soc*. 2003;51:314-322.
104. Verghese J, Holtzer R, Lipton RB, et al. Quantitative gait markers and incident fall risk in older adults. *J Gerontol A Biol Sci Med Sci*. 2009;64:896-901.
105. Kressig RW, Gregor RJ, Oliver A, et al. Temporal and spatial features of gait in older adults transitioning to frailty. *Gait Posture*. 2004;20:30-35.

106. Abellan van Kan G, Rolland Y, Andrieu S, et al. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force. *J Nutr Health Aging*. 2009;13:881-889.
107. Elble RJ, Thomas SS, Higgins C, et al. Stride-dependent changes in gait of older people. *J Neurol*. 1991;238:1-5.
108. Blanke DJ, Hageman PA. Comparison of gait of young men and elderly men. *Phys Ther*. 1989;69:144-148.
109. Watelain E, Barbier F, Allard P, et al. Gait pattern classification of healthy elderly men based on biomechanical data. *Arch Phys Med Rehabil*. 2000;81:579-586.
110. Oberg T, Karsznia A, Oberg K. Basic gait parameters: reference data for normal subjects, 10-79 years of age. *J Rehabil Res Dev*. 1993;30:210-223.
111. Stolze H, Friedrich HJ, Steinauer K, et al. Stride parameters in healthy young and old women--measurement variability on a simple walkway. *Exp Aging Res*. 2000;26:159-168.
112. DeVita P, Hortobagyi T. Age causes a redistribution of joint torques and powers during gait. *J Appl Physiol* (1985). 2000;88:1804-1811.
113. Terrier P, Schutz Y. Variability of gait patterns during unconstrained walking assessed by satellite positioning (GPS). *Eur J Appl Physiol*. 2003;90:554-561.
114. Jordan K, Challis JH, Newell KM. Walking speed influences on gait cycle variability. *Gait Posture*. 2007;26:128-134.
115. Terrier P, Turner V, Schutz Y. GPS analysis of human locomotion: further evidence for long-range correlations in stride-to-stride fluctuations of gait parameters. *Hum Mov Sci*. 2005;24:97-115.
116. Owings TM, Grabiner MD. Variability of step kinematics in young and older adults. *Gait Posture*. 2004;20:26-29.
117. Callisaya ML, Blizzard L, Schmidt MD, et al. Ageing and gait variability--a population-based study of older people. *Age Ageing*. 2010;39:191-197.
118. Grabiner PC, Biswas ST, Grabiner MD. Age-related changes in spatial and temporal gait variables. *Arch Phys Med Rehabil*. 2001;82:31-35.
119. Faude O, Donath L, Roth R, et al. Reliability of gait parameters during treadmill walking in community-dwelling healthy seniors. *Gait Posture*. 2012;36:444-448.

120. Galna B, Lord S, Rochester L. Is gait variability reliable in older adults and Parkinson's disease? Towards an optimal testing protocol. *Gait Posture*. 2013;37:580-585.
121. Atkinson G, Nevill AM. Statistical methods for assessing measurement error (reliability) in variables relevant to sports medicine. *Sports Med*. 1998;26:217-238.
122. Safrit MJ, Wood TM. *Measurement concepts in physical education and exercise science*. Champaign, Ill.: Human Kinetics Books; 1989.
123. van Iersel MB, Benraad CE, Rikkert MG. Validity and reliability of quantitative gait analysis in geriatric patients with and without dementia. *J Am Geriatr Soc*. 2007;55:632-634.
124. Bilney B, Morris M, Webster K. Concurrent related validity of the GAITRite walkway system for quantification of the spatial and temporal parameters of gait. *Gait Posture*. 2003;17:68-74.
125. Paterson KL, Hill KD, Lythgo ND, et al. The reliability of spatiotemporal gait data for young and older women during continuous overground walking. *Arch Phys Med Rehabil*. 2008;89:2360-2365.
126. Montero-Odasso M, Muir SW, Speechley M. Dual-task complexity affects gait in people with mild cognitive impairment: the interplay between gait variability, dual tasking, and risk of falls. *Arch Phys Med Rehabil*. 2012;93:293-299.
127. Beauchet O, Freiburger E, Annweiler C, et al. Test-retest reliability of stride time variability while dual tasking in healthy and demented adults with frontotemporal degeneration. *J Neuroeng Rehabil*. 2011;8:37.
128. Wittwer JE, Webster KE, Hill K. Reproducibility of gait variability measures in people with Alzheimer's disease. *Gait Posture*. 2013;38:507-510.
129. Schaafsma JD, Giladi N, Balash Y, et al. Gait dynamics in Parkinson's disease: relationship to Parkinsonian features, falls and response to levodopa. *J Neurol Sci*. 2003;212:47-53.
130. Besier TF, Sturnieks DL, Alderson JA, et al. Repeatability of gait data using a functional hip joint centre and a mean helical knee axis. *J Biomech*. 2003;36:1159-1168.
131. Maynard V, Bakheit AM, Oldham J, et al. Intra-rater and inter-rater reliability of gait measurements with CODA mpx30 motion analysis system. *Gait Posture*. 2003;17:59-67.
132. Dingwell JB, Cusumano JP, Cavanagh PR, et al. Local dynamic stability versus kinematic variability of continuous overground and treadmill walking. *J Biomech Eng*. 2001;123:27-32.

133. Frenkel-Toledo S, Giladi N, Peretz C, et al. Treadmill walking as an external pacemaker to improve gait rhythm and stability in Parkinson's disease. *Mov Disord.* 2005;20:1109-1114.
134. Owings TM, Grabiner MD. Measuring step kinematic variability on an instrumented treadmill: how many steps are enough? *J Biomech.* 2003;36:1215-1218.
135. Parvataneni K, Ploeg L, Olney SJ, et al. Kinematic, kinetic and metabolic parameters of treadmill versus overground walking in healthy older adults. *Clin Biomech (Bristol, Avon).* 2009;24:95-100.
136. Wass E, Taylor NF, Matsas A. Familiarisation to treadmill walking in unimpaired older people. *Gait Posture.* 2005;21:72-79.
137. Rosenblatt NJ, Grabiner MD. Measures of frontal plane stability during treadmill and overground walking. *Gait Posture.* 2010;31:380-384.
138. Danion F, Varraine E, Bonnard M, et al. Stride variability in human gait: the effect of stride frequency and stride length. *Gait Posture.* 2003;18:69-77.
139. Yamasaki M, Sasaki T, Torii M. Sex difference in the pattern of lower limb movement during treadmill walking. *Eur J Appl Physiol Occup Physiol.* 1991;62:99-103.
140. Holt KG, Hamill J, Andres RO. Predicting the minimal energy costs of human walking. *Med Sci Sports Exerc.* 1991;23:491-498.
141. Holt KJ, Jeng SF, Rr RR, et al. Energetic Cost and Stability During Human Walking at the Preferred Stride Velocity. *J Mot Behav.* 1995;27:164-178.
142. Wuehr M, Schniepp R, Pradhan C, et al. Differential effects of absent visual feedback control on gait variability during different locomotion speeds. *Exp Brain Res.* 2013;224:287-294.
143. Dingwell JB, Marin LC. Kinematic variability and local dynamic stability of upper body motions when walking at different speeds. *J Biomech.* 2006;39:444-452.
144. Beauchet O, Annweiler C, Lecordroch Y, et al. Walking speed-related changes in stride time variability: effects of decreased speed. *J Neuroeng Rehabil.* 2009;6:32.
145. Moe-Nilssen R, Helbostad JL. Interstride trunk acceleration variability but not step width variability can differentiate between fit and frail older adults. *Gait Posture.* 2005;21:164-170.



146. Oberg T, Karsznia A, Oberg K. Joint angle parameters in gait: reference data for normal subjects, 10-79 years of age. *J Rehabil Res Dev.* 1994;31:199-213.
147. Moe-Nilssen R, Helbostad JL. Estimation of gait cycle characteristics by trunk accelerometry. *J Biomech.* 2004;37:121-126.
148. Beauchet O, Allali G, Launay C, et al. Gait variability at fast-pace walking speed: a biomarker of mild cognitive impairment? *J Nutr Health Aging.* 2013;17:235-239.
149. Nieuwboer A, Kwakkel G, Rochester L, et al. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. *J Neurol Neurosurg Psychiatry.* 2007;78:134-140.
150. Repp BH. Sensorimotor synchronization: a review of the tapping literature. *Psychon Bull Rev.* 2005;12:969-992.
151. Zatorre RJ, Chen JL, Penhune VB. When the brain plays music: auditory-motor interactions in music perception and production. *Nat Rev Neurosci.* 2007;8:547-558.
152. Wittwer JE, Webster KE, Hill K. Music and metronome cues produce different effects on gait spatiotemporal measures but not gait variability in healthy older adults. *Gait Posture.* 2013;37:219-222.
153. Van Peppen RP, Kwakkel G, Wood-Dauphinee S, et al. The impact of physical therapy on functional outcomes after stroke: what's the evidence? *Clin Rehabil.* 2004;18:833-862.
154. Rossignol S, Jones GM. Audio-spinal influence in man studied by the H-reflex and its possible role on rhythmic movements synchronized to sound. *Electroencephalogr Clin Neurophysiol.* 1976;41:83-92.
155. Chen JL, Penhune VB, Zatorre RJ. The role of auditory and premotor cortex in sensorimotor transformations. *Ann N Y Acad Sci.* 2009;1169:15-34.
156. Styns F, van Noorden L, Moelants D, et al. Walking on music. *Hum Mov Sci.* 2007;26:769-785.
157. Thaut MH, Miltner R, Lange HW, et al. Velocity modulation and rhythmic synchronization of gait in Huntington's disease. *Mov Disord.* 1999;14:808-819.
158. Baker K, Rochester L, Nieuwboer A. The effect of cues on gait variability--reducing the attentional cost of walking in people with Parkinson's disease. *Parkinsonism Relat Disord.* 2008;14:314-320.

159. Sheridan PL, Hausdorff JM. The role of higher-level cognitive function in gait: executive dysfunction contributes to fall risk in Alzheimer's disease. *Dement Geriatr Cogn Disord*. 2007;24:125-137.
160. Ebersbach G, Heijmenberg M, Kindermann L, et al. Interference of rhythmic constraint on gait in healthy subjects and patients with early Parkinson's disease: evidence for impaired locomotor pattern generation in early Parkinson's disease. *Mov Disord*. 1999;14:619-625.
161. Arias P, Cudeiro J. Effects of rhythmic sensory stimulation (auditory, visual) on gait in Parkinson's disease patients. *Exp Brain Res*. 2008;186:589-601.
162. Haley SM, Fragala-Pinkham MA. Interpreting change scores of tests and measures used in physical therapy. *Phys Ther*. 2006;86:735-743.
163. Kobsar D, Olson C, Paranjape R, et al. Evaluation of age-related differences in the stride-to-stride fluctuations, regularity and symmetry of gait using a waist-mounted tri-axial accelerometer. *Gait Posture*. 2014;39:553-557.
164. Brach JS, Perera S, VanSwearingen JM, et al. Challenging gait conditions predict 1-year decline in gait speed in older adults with apparently normal gait. *Phys Ther*. 2011;91:1857-1864.
165. Rosner B. *Fundamentals of biostatistics*. 4th ed. Belmont, Calif.: Duxbury Press; 1995.
166. Konig N, Singh NB, von Beckerath J, et al. Is gait variability reliable? An assessment of spatio-temporal parameters of gait variability during continuous overground walking. *Gait Posture*. 2014;39:615-617.
167. Thies SB, Richardson JK, Ashton-Miller JA. Effects of surface irregularity and lighting on step variability during gait: a study in healthy young and older women. *Gait Posture*. 2005;22:26-31.
168. Kressig RW, Beauchet O, European GNG. Guidelines for clinical applications of spatio-temporal gait analysis in older adults. *Aging Clin Exp Res*. 2006;18:174-176.
169. Schrage MA, Kelly VE, Price R, et al. The effects of age on medio-lateral stability during normal and narrow base walking. *Gait Posture*. 2008;28:466-471.
170. den Otter AR, Geurts AC, Mulder T, et al. Speed related changes in muscle activity from normal to very slow walking speeds. *Gait Posture*. 2004;19:270-278.
171. Frenkel-Toledo S, Giladi N, Peretz C, et al. Effect of gait speed on gait rhythmicity in Parkinson's disease: variability of stride time and swing time respond differently. *J Neuroeng Rehabil*. 2005;2:23.

172. Kuo AD, Donelan JM. Dynamic principles of gait and their clinical implications. *Phys Ther.* 2010;90:157-174.
173. Hausdorff JM, Peng CK, Ladin Z, et al. Is walking a random walk? Evidence for long-range correlations in stride interval of human gait. *J Appl Physiol* (1985). 1995;78:349-358.
174. VanSwearingen JM, Studenski SA. Aging, motor skill, and the energy cost of walking: implications for the prevention and treatment of mobility decline in older persons. *J Gerontol A Biol Sci Med Sci.* 2014;69:1429-1436.
175. Grieve DW, Gear RJ. The relationships between length of stride, step frequency, time of swing and speed of walking for children and adults. *Ergonomics.* 1966;9:379-399.
176. Zarrugh MY, Todd FN, Ralston HJ. Optimization of energy expenditure during level walking. *Eur J Appl Physiol Occup Physiol.* 1974;33:293-306.
177. Sekiya N, Nagasaki H, Ito H, et al. Optimal walking in terms of variability in step length. *J Orthop Sports Phys Ther.* 1997;26:266-272.
178. Kurosawa K. Effects of various walking speeds on probe reaction time during treadmill walking. *Percept Mot Skills.* 1994;78:768-770.
179. Sekiya N, Nagasaki H. Reproducibility of the walking patterns of normal young adults: test-retest reliability of the walk ratio(step-length/step-rate). *Gait Posture.* 1998;7:225-227.
180. Nagasaki H, Itoh H, Hashizume K, et al. Walking patterns and finger rhythm of older adults. *Percept Mot Skills.* 1996;82:435-447.
181. Murray MP, Sepic SB, Gardner GM, et al. Walking patterns of men with parkinsonism. *Am J Phys Med.* 1978;57:278-294.
182. Rota V, Perucca L, Simone A, et al. Walk ratio (step length/cadence) as a summary index of neuromotor control of gait: application to multiple sclerosis. *Int J Rehabil Res.* 2011;34:265-269.
183. Wu T, Chan P, Hallett M. Effective connectivity of neural networks in automatic movements in Parkinson's disease. *Neuroimage.* 2010;49:2581-2587.
184. Jahn K, Deutschlander A, Stephan T, et al. Brain activation patterns during imagined stance and locomotion in functional magnetic resonance imaging. *Neuroimage.* 2004;22:1722-1731.

- 185.** Shibasaki H, Fukuyama H, Hanakawa T. Neural control mechanisms for normal versus parkinsonian gait. *Prog Brain Res.* 2004;143:199-205.
- 186.** Egerton T, Danoudis M, Huxham F, et al. Central gait control mechanisms and the stride length - cadence relationship. *Gait Posture.* 2011;34:178-182.
- 187.** Repp BH, Su YH. Sensorimotor synchronization: a review of recent research (2006-2012). *Psychon Bull Rev.* 2013;20:403-452.
- 188.** Dickstein R, Plax M. Metronome rate and walking foot contact time in young adults. *Percept Mot Skills.* 2012;114:21-28.
- 189.** Drew T, Prentice S, Schepens B. Cortical and brainstem control of locomotion. *Prog Brain Res.* 2004;143:251-261.
- 190.** Matsuyama K, Mori F, Nakajima K, et al. Locomotor role of the corticoreticular-reticulospinal-spinal interneuronal system. *Prog Brain Res.* 2004;143:239-249.